

Ref. 1



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June 6, 2006

C. Scott Tocher, Interim Counsel
California Institute for Regenerative Medicine
210 King Street
San Francisco, California
94107

RE: Comment on the CIRM IP Policy for Non-Profit Regulations

Dear Mr. Tocher,

To ensure that the promises of Proposition 71 are met and that any public funded cures and treatments are affordable and accessible for all Californians, the Foundation for Taxpayer and Consumer Rights is submitting these comments on the proposed California Institute For Regenerative Medicine's Intellectual Property Policy for Non-Profit Organizations (17 Cal. Code of Regs. §100300 to §100310). The first comments are substantive and make suggestions that would implement better the purposes outlined in the Initial Statement of Reasons for Adoption. The second category of comments is technical and would make the language more precise, helping to clarify the regulations' meaning.

Substantive Comments

REASONABLE PRICING: The rationale for §1000306 Licensing CIRM Funded Patented Inventions states, "CIRM seeks to ensue that licensees of CIRM-funded patented inventions obtain the appropriate scope of rights necessary for them to develop potential applications of the invention while optimizing the public good through the widespread use of the invention."

One purpose for §100310 March-In Rights is to provide direction as to when CIRM will act to intervene and take back an exclusive license. One ground is "failure by the licensee/grantee to adhere to requirements for public use." The rationale for the section includes provisions "to prevent the underutilization of CIRM-funded inventions." Grounds given to march in include: "to meet requirements for public use" or "failure to provide adequate availability of resultant products for the public use."

Unless resultant drugs or therapies are priced reasonably, public good will not be optimized nor will there be widespread use of the invention. If therapies and drugs are priced unreasonably "requirements for public use" will not be met. If drugs or therapies are priced unreasonably, there will certainly be a "failure to provide adequate availability of resultant products for the public use."

Thus, while the regulations and Statement of Reasons as noticed through the Office of Administrative Law process do already provide CIRM an implicit responsibility to intervene in the event of unreasonable pricing, this implicit right must be explicitly spelled out in the regulations. Moreover, because of CIRM's limited staff and emphasis on scientific research, the march-in rights should be assigned to the California Attorney General. Therefore we propose the following new language:

§100306 (f) Grantee organizations shall negotiate relevant and specific grounds for modification or termination of the license. Examples would include failure to meet agreed upon commercialization benchmarks, failure to keep the licensed invention reasonably accessible to the public for research purposes, failure to make the resultant therapies available to the public at a reasonable price, and failure to reasonably meet the agreed-upon plan for access to resultant therapies as described in subdivision (d) of this regulation. Reasonable price takes into account the actual cost of the therapy's development and the public's investment.

§100310 (a) With regard to CIRM funded-patented inventions, CIRM and the attorney general shall have the right...

(a)(3) To meet requirements for public use including that therapies be priced reasonably and the requirements have not been satisfied by the grantee organization or its licensee. Reasonable price takes into account the actual cost of the therapy's development and the public's investment ;

PATENT POOL: The purpose of §100306 (b) "requires grantees to negotiate nonexclusive licenses whenever possible". The rationale cites as a reason for this section "optimizing the public good through widespread use of the invention" and notes that "CIRM encourages the use of non-exclusive licenses." A patent pool would better promote these ends. FTCTC proposes the following new language:

§100306 (b) Grantee organizations shall negotiate non-exclusive licenses of CIRM-funded inventions whenever possible. To facilitate such licensing, grantees shall place CIRM-funded inventions in a patent pool unless an exclusive license is necessary to provide economic incentives required to enable commercial development and availability of the inventions.

REVENUE SHARING: The rationale for §100308 is that "CIRM seeks to obtain a financial return on the public's research investment." That return begins after revenues cross a threshold of \$500,000. CIRM expects 25 percent of net revenues after the threshold is reached. However, net revenues are defined as gross revenue, minus the inventor's share and direct costs incurred in the generation and protection of patents. Moreover, exclusive licensees generally reimburse the institution for patent costs. Therefore the threshold is too high and unnecessarily diminishes the state's return. The threshold should be \$100,00. FTCTC proposes the following language:

§100308 (b) ...The threshold amount is \$100,000 (in the aggregate) multiplied...

RESEARCH EXEMPTION AND BIOMEDICAL MATERIALS: The rationale for §100304 asserts, "In order to achieve the maximum public benefit, data and biomedical materials (including research tools) should be as freely available as possible in the public domain. " Frequently CIRM officials have stressed the importance of widespread sharing, however, the regulations don't recognize that valuable research will take place outside of California. If California expects to be a leader in stem cell research, we must craft a policy that fosters the exchange of information with stem cell scientists around the world. FTCCR proposes the following new language:

§100304. Grantees shall share biomedical materials described in published scientific articles for research purposes in California within 60 days of receipt of a request and without bias as to the affiliation of the requestor unless otherwise legally precluded. Following the principle of reciprocity, grantees shall share biomedical materials on the same basis with any non-California research institution that shares biomedical materials with California institutions. Under special circumstances...

§100307. Grantee organizations agree that California research institutions may use their CIRM-funded patented inventions for research purposes at no cost. Following the principle of reciprocity, grantee organizations also agree that any non-California research institution may use CIRM-funded patented inventions for research purposes at no cost if the non-California institution makes its patented inventions available for research at no cost to California research institutions. Grantee organizations shall ensure...

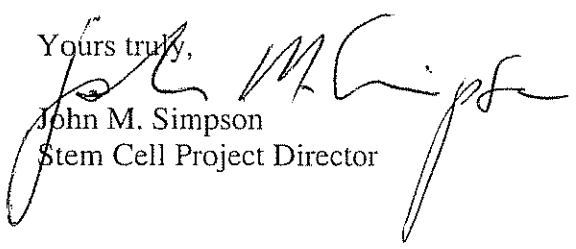
Technical comments

In the IP policy approved by the ICOC on Feb. 10, Chapter I listed a number of abbreviations and definitions. Many of the definitions were incorporated in the regulations submitted to the OAL process, but not all. Among abbreviations that appear in the regulation's text without definition are NGA (Page 3, line 9), CELR (Page 9, line 7) and SPO (Page 13, line 17).

§100308 (a) states "Grantee organizations shall share a fraction of any net revenues with the inventor(s) in accordance with their established policies." The next sentence reads, "Net revenues are defined as gross revenues minus the inventor's share and the direct costs incurred in the generation and protection of patents from which revenues are received." Together these sentences give incompatible definitions of the revenue that the inventor shares. Surely this must be a typo and the first sentence should read, "Grantee organizations shall share a fraction of any gross revenues with the inventor(s)..." Or, perhaps, even, "Grantee organizations shall share a fraction of any revenues with the inventor(s) ..."

Thank you for your consideration.

Yours truly,


John M. Simpson
Stem Cell Project Director

June 15, 2006

BY ELECTRONIC MAIL TO NONPROFITPREGS@CIRM.CA.GOV

Mr. C. Scott Tocher
Interim Counsel
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Comments to Proposed CIRM Regulation Entitled: Intellectual Property Policy for Non-Profit Organizations, [California Code of Regulations, Title 17. — Public Health, Division 4 — California Institute For Regenerative Medicine, Chapter 3]

Dear Mr. Tocher:

The California Healthcare Institute (CHI) welcomes this opportunity to comment on the California Institute for Regenerative Medicine's (CIRM) interim regulations addressing Intellectual Property Policy for Non-Profit Organizations (IPPNPO) as approved by the Independent Citizens' Oversight Committee (ICOC) on February 10, 2006. CHI represents the full biomedical sector of the California economy; our members include more than 250 of California's leading life sciences companies, universities, and academic research institutions.

California's highly-developed infrastructure -- including basic science, venture capital, commercial life sciences companies, along with the many support services (e.g. legal, accounting, architectural) essential to transforming scientific discoveries into products -- is the reason our state is the global leader in biotechnology. And it is the reason that public funding of embryonic stem cell research in California can exert enormous leverage. No other state in America -- no other nation in the world -- has the people and experience to capitalize on this new science as quickly as California.

As the advocate for California's biomedical research and development community, CHI appreciates the ICOC's efforts to develop an intellectual property policy that conforms to the purpose and intent of Proposition 71, the California Stem Cell Research and Cures Act (Prop 71). The focus of Prop 71 is to support human embryonic stem cell research with the goal of discovering new diagnostics, treatments and therapies. We therefore support the stated objectives of the IPPNPO to "promote sharing of all types of intellectual property created as a consequence of CIRM funding for use in research conducted by both academic and commercial research and development organizations" and "to facilitate the commercialization of CIRM-funded discoveries without impeding the progress of stem cell research."¹

¹ CIRM Intellectual Property Policy for Non-Profit Organizations, approved by the ICOC on February 10, 2006. pg 4-5.

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At the same time, however, CHI is concerned with the IPPNPO objective “to provide a financial benefit to the State of California through revenue sharing in the event that CIRM-funded discoveries lead to valuable diagnostic and/or medical therapies” and specific IPPNPO provisions addressing pricing and access requirements in technology transfer agreements.² Far from promoting technology transfer and commercial product development, these provisions are likely to discourage commercial interest. Because commercialization is essential for the development and production of new medicines, CHI believes that the goal of the IPPNPO should be to *minimize* barriers to technology transfer. Moreover, while we strongly support policies to improve access to advanced medicine, we maintain that IP policies and regulations are not the proper venue for addressing the issues of access and cost.

CHI has consistently encouraged policies to regulate transaction among academic institutions and commercial companies based on the federal Bayh-Dole Act (P.L. 96-517, Amendments to the Patent and Trademark Act).³ While the IPPNPO is generally modeled on federal laws governing technology transfer⁴, it includes several provisions that diverge significantly:

- Product pricing and access provisions that permit licensing “only to organizations with plans to provide access to resultant therapies and diagnostics for uninsured California patients” and only if “licensees will agree to provide to patients whose therapies and diagnostics will be purchased in California by public funds the therapies and diagnostics at a cost not to exceed the federal Medicaid price”;⁵
- March-in rights and grounds for termination of licenses that may be exercised if the pricing and access provisions referenced above are not adhered to;⁶
- Recoupment and revenue-sharing provisions that, beyond a threshold amount and after payments to investors, require grantees to pay 25% of revenues received under a license agreement to the State of California for deposit into the State’s General Fund;⁷ and
- Broad, vague and ambiguous requirements that CIRM-funded inventions must be made available, by grantee organizations and licensees, for research purposes at no cost.⁸

During the past thirty years, California biotechnology companies have licensed hundreds of inventions from academic institutions. The lesson from this collective experience is that stakeholders – researchers and research organizations, industry and other licensees, and venture

² Ibid

³ See Statement of David L. Gollaher, Ph.D., President and CEO, California Healthcare Institute (CHI) before the Joint Informational Hearing of the Senate Health and Human Services Committee and Assembly Health Committee, Sept. 15, 2004

⁴ Including, in addition to Bayh-Dole, P.L. 96-418, the Stevenson-Wydler Technology Innovation Act (Stevenson-Wydler), as amended

⁵ Proposed Title 17 of California Code of Regulations, section 100306(d)

⁶ Proposed Title 17 of California Code of Regulations, section 100310(a)(2) and section 100306(f)

⁷ Proposed Title 17 of California Code of Regulations, section 100308(b)

⁸ Proposed Title 17 of California Code of Regulations, section 100307 and section 100306(f)

capital investors – value transparency and predictability in licensing and technology transfer agreements. Biotechnology is inherently risky. Any aspect of a technology transfer contract that increases risk, particularly by adding an element of uncertainty, makes it less attractive to potential partners and investors and thus reduces the prospects for successful commercial collaboration.

We address in detail our concerns regarding specific provisions below.

The Life Sciences Business Model and the Impact of Bayh-Dole

Intense competition for investment capital places enormous pressures on biopharmaceutical firms, whose products require years of testing to meet U.S. Food and Drug Administration (FDA) standards. On average, it takes 10 to 15 years and more than \$800 million to develop a potential new medicine from a basic research discovery to a product approved by the FDA. Before FDA product approval, the value of a biomedical company depends on its patents – its intellectual property. In fact, for many of the smaller firms that comprise the majority of the biomedical industry, and whose products and technologies are still in pipeline, IP is sometimes their only real asset. The biotechnology industry in California rests fundamentally on IP.

Bayh-Dole, Stevenson-Wydler, and other federal policies regulating intellectual property and technology transfer have been important to the success of California's biomedical research and development enterprise.

Prior to Bayh-Dole --

"[T]he government [generally] retained title to inventions made with government support whether the research was performed in federal laboratories, in universities, or by individual companies. Licenses to use government patents were then negotiated with firms either on a non-exclusive basis (meaning additional companies could use the technology) or, more rarely, for the exclusive use by one manufacturer. However, it was widely argued that without title (or at least an exclusive license) to an invention and the protection it conveys, a company would not invest the additional, and substantial time and money necessary to commercialize a product or process for the marketplace."⁹

Enactment of Bayh-Dole, therefore, created a "single, uniform national policy designed to cut down on bureaucracy and **encourage private industry to utilize government financed inventions through the commitment of the risk capital necessary to develop such inventions to the point of commercial application.**"¹⁰

The licensing and technology transfer mechanisms of Bayh-Dole have had an especially significant impact on the life sciences. In California alone, since Bayh-Dole's enactment in

⁹ Congressional Research Service (CRS) Report RL32076, *The Bayh-Dole Act: Selected Issues in Patent Policy and the Commercialization of Technology*, by Wendy Schacht. Updated June 10, 2005. p 2.

¹⁰ House Committee on the Judiciary, *Report to Accompany H.R. 6933*, 96th Congress, 2nd Session, H.Rept. 96-1307, Part 1, p3. Emphasis added.

1980, the state's leading academic and non-profit research institutions have spun out over 600 biomedical companies through technology transfer agreements.¹¹

Given the federal technology transfer model's record of success in advancing biomedical research, development, and commercialization, CHI urges the ICOC to adopt an IPPNPO that is more closely in line with federal policy. Where the interim IPPNPO policy differs, we believe that the record of debate, consideration, decision-making, and experience at the federal level offers evidence of the barriers and disincentives that an overly restrictive or ambiguous policy can create.

i. Proposed Title 17 of California Code of Regulations, Section 100306(d)

CHI is concerned that the ICOC may be inappropriately using the IPPNPO to address health care access and pricing issues by requiring exclusive licensing of CIRM-funded inventions "only to organizations with plans to provide access to resultant therapies and diagnostics for uninsured California patients" and only if "licensees will agree to provide to patients whose therapies and diagnostics will be purchased in California by public funds the therapies and diagnostics at a cost not to exceed the federal Medicaid price." While improving health care access and affordability are important goals, they were not the objective of Prop 71 and should, therefore, not be the subject of policies and regulations pertaining to Prop 71.

Indeed, CHI strongly believes that a stated purpose of Prop 71 – to "[i]mprove the California health care system and reduce the long-term health care cost burden on California through the development of therapies that treat diseases and injuries with the ultimate goal to cure them" assumes that CIRM-funded research and resulting innovation will directly address these goals.¹² Requirements included in the draft IPPNPO would discourage commercial collaboration, technology transfer and licensing by (a) reducing the rate of return on CIRM-related deals in comparison to other academic-industry transactions, and (b) increasing investors' financial risk by imposing state price regulation on downstream products. Considering biotechnology's long product lead times, price regulation makes it all the more difficult to project return on investment.

Experience at the federal level confirms these concerns. Technology transfer and licensing policies at the National Institutes of Health (NIH) attempted to incorporate "fair pricing" requirements, with poor results. According to a report by the Congressional Research Service (CRS) --

Prior to 1995, NIH had included what was known as a "fair pricing clause" in its cooperative research and development agreements [CRADA] and many licensing arrangements. In 1989, the Public Health Service (PHS) instituted a policy addressing the pricing of products resulting from a government-owned patent licensed by NIH on an exclusive basis to industry or an invention jointly developed with industry under a CRADA and then licensed exclusively to the collaborator. ...

¹¹ Source: PricewaterhouseCoopers/California Healthcare Institute surveys, 2002 and 2003

¹² Text of Proposition 71, Sec. 3, "Purpose and Intent"

The clause was removed in 1995 at the request of Dr. Harold Varmus, Director of NIH, after a review of the situation and several public hearings. He concluded that the evidence indicated "**...the pricing clause has driven industry away from potentially beneficial scientific collaborations with PHS scientists without providing an offsetting benefit to the public.**" While sharing concerns over the "potential inaccessibility" of drugs due to costs, "**NIH [agreed] with the consensus of the advisory panels that enforcement of a pricing clause would divert NIH from its primary research mission and conflict with its statutory mission to transfer promising technologies to the private sector for commercialization.**" A study by the Department of Health and Human Services Inspector General found that companies viewed the clause as a major problem in the NIH CRADA approach. Opponents of the clause argued that the **uncertainty of the pricing clause exacerbated a process already fraught with risk.** According to industry sources, **not knowing what the determination of "fair" pricing would be at the end of a long and expensive research, development, and commercialization process was a strong deterrent to entering into cooperative arrangements.** Many of the pharmaceutical and biotechnology companies declined to undertake CRADAs. Some firms even declined opportunities for joint clinical trials with NIH in anticipation of future price control demands.¹³ (emphasis added)

Based on these findings, CHI is concerned that the IPPNPO pricing and access provisions would similarly divert CIRM from its primary missions as outlined by Prop 71. Accordingly, CHI strongly urges the ICOC to remove Section 100306(d) from the final IPPNPO.

ii. Proposed Title 17 of California Code of Regulations, Section 100310(a)(2) and Section 100306(f)

CHI is similarly concerned with the IPPNPO's grounds for termination of licenses and "march-in" rights, provisions and procedures, especially as they pertain to the pricing and access requirements addressed above. While based on provisions in Bayh-Dole, the IPPNPO differs notably by including among the circumstances for triggering march-in rights failure by licensees to adhere to pricing and/or access plans as described in the proposed Title 17 of California Code of Regulations, Section 100306(d).¹⁴ CHI maintains that these provisions present an additional disincentive to commercial collaboration.

Bayh-Dole march-in provisions do not include product costs as a triggering mechanism, nonetheless several attempts have been made to persuade the federal government to exercise march-in rights based on the premise that prices of certain pharmaceutical products developed with federal funding were "unreasonable." In each case, the NIH decided not to initiate march-in proceedings.¹⁵ This history suggests that the ICOC, CIRM and licensees of CIRM-funded institutions would almost certainly face calls for the state to exercise march-in rights. The result would be to add another layer of risk and uncertainty to academic-commercial transactions. CHI therefore suggests that the ICOC remove pricing and access as grounds for both the triggering of CIRM march-in rights and the termination of licenses.

¹³ Congressional Research Service (CRS) Report RL32324, *Federal R&D, Drug Discovery, and Pricing: Insights from the NIH-University-Industry Relationship*, by Wendy Schacht. March 16, 2004. p 15-16

¹⁴ P.L. 96-517, Section 203

¹⁵ See "NIH March-In position paper in the case of Xalatan" and "NIH March-In position paper in the case of Norvir" at http://www.ott.nih.gov/policy/policies_and_guidelines.html

CHI also requests, consistent with Bayh-Dole, that “public use” requirements addressed in Section 100310(a)(3) be clearly specified to minimize ambiguity and uncertainty.

Finally, CHI requests that the ICOC very carefully consider how to address march-in proceedings. At a minimum, the ICOC should establish detailed procedures that, in addition to the notice of determination and basis as provided in Section 100310(b), establish the right of the patent holder, licensee, and other interested stakeholders to submit information and arguments opposing and appealing any proposed march-in prior to final action.

iii. Proposed Title 17 of California Code of Regulations, Section 100308(b)

CHI acknowledges that an intent of the research funded by Prop 71 is to “[provide] an opportunity for the state to benefit from royalties, patents, and licensing fees that result from the research.”¹⁶ However, we question IPPNPO provisions that would require grantees to pay, beyond a threshold amount and after payments to inventors, 25% of revenues received under a license agreement to the State of California for deposit into the State’s General Fund. Beyond the request that, for the purposes of this section, the IPPNPO definition of “revenues” be clarified to exclude equity ownership, such as stock, stock options, etc., CHI suggests that direct revenue sharing and/or recoupment provisions may actually reduce the public benefit of Prop 71 funded research.

A CRS Report for Congress succinctly summarizes the decision at the federal level *not* to require direct recoupment provisions —

Providing universities, nonprofit institutions, and small businesses with title to patents arising from federally-funded R&D offers an incentive for cooperative work and commercial application. Royalties derived from intellectual property rights provide the academic community an alternative way to support further research and the business sector a means to obtain a return on their financial contribution to the endeavor. While the idea of recoupment was considered by the Congress in hearings on [Bayh-Dole] legislation, it was rejected as an unnecessary obstacle, one which would be perceived as an additional burden to working with the government. It was thought to be particularly difficult to administer. Instead, Congress accepted as satisfactory the anticipated payback to the country through increased revenues from taxes on profits, new jobs created, improved productivity, and economic growth. For example, according to the MIT Technology Licensing Office, 15% of the sales of licensed products derived from federally funded university research is returned to the government in the form of income taxes, payroll taxes, capital gains taxes, and corporate income taxes. This is estimated to be 6 times the royalties paid by companies to the universities. The emergence of the biotechnology industry and the development of new therapeutics to improve health care are other prominent indications of such benefits. These benefits have been considered more important than the initial cost of the technology to the government or any potential unfair advantage.¹⁷

¹⁶ Text of Proposition 71, Sec. 3, “Purpose and Intent”

¹⁷ *The Bayh-Dole Act: Selected Issues in Patent Policy and the Commercialization of Technology*, p. 14

CHI suggests that the financial benefits to the state from CIRM-funded research and subsequent technology transfer and product commercialization will come from job creation, exports, increased income taxes, payroll taxes, capital gains taxes, corporate income taxes – in short from a broad range of economic factors. We further suggest that a recoupment policy will, in fact, divert grantees' financial resources from additional research activities that would otherwise be possible. We therefore request that the ICOC reconsider Section 100308(b) of the interim IPPNPO.

iv. Proposed Title 17 of California Code of Regulations, Section 100307

CHI opposes the draft IPPNPO's extremely broad and unprecedented research use exemption provision. While CHI shares the objective of ensuring that CIRM-funded inventions are made broadly available to the California research community, the provision in the IPPNPO, as written, may have several negative unintended consequences.

First, it eliminates any possibility that a CIRM-funded research tool will be commercialized, because it requires that any licensee make such a research tool available to all California researchers at no cost. If all California customers must be served free, there is no commercial opportunity in embryonic stem cell related research tools. Second, it creates discriminatory treatment of the substantial research tools segment of the California life sciences industry. Prop 71 and CIRM fully recognize that commercial incentives must be preserved to get CIRM-supported therapies and diagnostics to patients in need. The premise that research and development is a two part process, with academic institutions performing basic research and commercial companies conducting applied research, development and commercialization, is fundamental to Prop 71. CHI holds that this principle should apply equally to research tools because commercialization of such inventions accelerates their broad dissemination to the research and commercial communities. Indeed, the academic and non-profit research institutes that initially develop research tools have neither the resources nor the facilities to produce and distribute them in the quantity necessary, making commercialization a fundamentally essential component to research tools dissemination. Just as therapies must reach patients to achieve health benefits, so too must new research tools for stem cell isolation, characterization, and differentiation reach investigators for stem cell research to advance at the fastest possible rate. Finally, the inclusion of such a sweeping research use provision in the IPPNPO sets a dangerous precedent at a time when research use policy is currently being debated in many forums. Given these factors, CHI urges the ICOC to use extreme caution before enacting any research use provisions.

In the rationale for Sec. 100307 outlined in the Statement of Reasons, reference is made to the Patent Act of 1952 and its lack of a "generally applicable research exemption."¹⁸ While exemptions from patent enforcement are rare in U.S. patent law, there are in fact two operative types of research use exemptions that will apply to CIRM grantees even in the absence of any research use provision in the IPPNPO.

¹⁸ CIRM "Initial Statement of Reasons for the Proposed Adoption of Intellectual Property Regulations for Non-Profit Organizations", p 9.

One exemption is the judicially created common law research-use exemption. This exemption provides that it is not an act of infringement to make and use a patented invention if the use is limited to research or experimentation and the user does not obtain any commercial advantage or benefit. There have been only a handful of cases in the 200-year history of this exemption, but in those cases the courts have interpreted this exemption narrowly. In *Madey v. Duke*, the Court of Appeals for the Federal Circuit held that activities that could be construed to have a business-related objective (*e.g.*, publishable research to further a university's prestige, image, and ability to bring in grant money) are considered to be outside the scope of a research use exemption.¹⁹ Thus, academic researchers may be outside the scope of exemption if their activities further the interests of their institutions, such as attracting researchers or securing research grants. As a practical matter however, a patent owner will generally not enforce his patent against a researcher if the research activities in question do not damage the patent owner's commercial interests. While the *Madey v. Duke* decision has raised many concerns in the academic community, a recent study commissioned by the National Academies indicates few instances where patents have constrained commercial or academic biomedical research, even in areas of substantial commercial interest.²⁰ This is true even in the post *Madey v. Duke* environment despite some reported activity aimed at influencing academic research or publication.

A second type of research exemption is a part of the Hatch-Waxman Act of 1984.²¹ It allows making and using a patented pharmaceutical compound or device to collect data for submission to a U.S. government regulatory agency. This is a "safe harbor" for individuals or entities making and using patented materials for uses reasonably related to the development and submission of information to the government (*e.g.*, the FDA). The U.S. Supreme Court recently interpreted this provision very broadly, creating a large statutory drug development-specific research use provision in U.S. law.²² This statutory exemption as well as the common law research use exemption will apply to CIRM grantees absent any additional research use provision in the IPPNPO.

We also point out that researchers can avoid infringement liability by obtaining authorization from patent holders for use of an invention in research.

Finally, it should be noted that good non-patent related alternatives to the research use provision exist. NIH, for example, uses its Research Tool Guidelines to effectively encourage broad dissemination of NIH-funded research tools.²³ Importantly, the NIH approach focuses on the goal of broad access and preserves the flexibility to use commercial forces where they are the

¹⁹ JOHN M.J. MADEY, Plaintiff-Appellant, v. DUKE UNIVERSITY, Defendant-Appellee. UNITED STATES COURT OF APPEALS FOR THE FEDERAL CIRCUIT. 307 F.3d 1351; 2002 U.S. App. LEXIS 20823; 64 U.S.P.Q.2D (BNA) 1737

²⁰ "Reaping the Benefits of Genomic and Proteomic Research: Intellectual Property Rights, Innovation, and Public Health", 2006. As available at <http://www.nap.edu/catalog/11487.html>

²¹ 35 U.S.C. §271(e)(1)

²² In decision on *Merck KGaA v. Integra LifeSciences I, Ltd.* Available at <http://www.supremecourtus.gov/opinions/04pdf/03-1237.pdf>

²³ See "NIH Principles and Guidelines for Sharing of Biomedical Resources" available at <http://ott.od.nih.gov/pdfs/64FR72090.pdf>

best means of achieving broad dissemination. That approach also does not risk undermining the core incentive structure that has motivated the development of so many important life science tools.

Given these factors, CHI suggests that Section 100307 of the IPPNPO be removed or significantly narrowed to acknowledge existing research use exemptions along with the importance and value of commercial research tools to CIRM-funded research, commercial collaboration, and product development. Otherwise, we are concerned that this provision, as written, would eliminate any incentive for private industry to make the additional investments necessary to bring CIRM-funded research-related IP to fruition. Without private sector investment in research innovations, stem cell research and the development of resulting new treatments and therapies will be constrained.

Similarly, CHI suggests that the requirement that grounds for termination of licenses include "failure to keep the licensed invention available to the public for research purposes" included in Section 100306(f) is, as written, vague, overbroad and ambiguous for the same reasons as mentioned above with regards to Section 100310(a)(3). Nor is that language seemingly consistent with the initial requirement of Section 100307, which addresses "California research institutions." Therefore, CHI requests that the ICOC remove or clarify this provision to better explain what purpose it is intended to serve (i.e. what other provisions of the regulations it is intended to support).

Conclusion

CHI appreciates this opportunity to comment on the interim CIRM Intellectual Property Policy for Non-Profit Organizations. We believe that a strong IPPNPO will advance CIRM-funded stem cell research and, ultimately, treatments for millions here in California and worldwide. This, in turn, will improve California's health care system, benefit the California economy, and further promote the state's biotechnology industry as a global leader. We hope that the ICOC will give careful consideration to our comments and incorporate them into the final IPPNPO.

In summary, to promote technology transfer and commercial collaboration on CIRM-funded inventions and to limit barriers to stakeholder participation in research, licensing, and commercialization, CHI suggests that the ICOC:

- Remove Section 100306(d), which permits licensing "only to organizations with plans to provide access to resultant therapies and diagnostics for uninsured California patients" and only if "licensees will agree to provide to patients whose therapies and diagnostics will be purchased in California by public funds the therapies and diagnostics at a cost not to exceed the federal Medicaid price".
- Remove Section 100310(a)(2), which sets pricing and access issues as conditions for the triggering of CIRM march-in rights.

- Clearly specify "public use" requirements addressed in Section 100310(a)(3) in order to minimize ambiguity and uncertainty.
- Remove pricing and access issues as grounds for modification or termination of licenses as provided in Section 100306(f).
- Remove or consider more effective and efficient alternatives to Section 100308(b), which establishes a direct revenue-sharing policy for CIRM-funded commercialized technologies.
- Remove or significantly narrow Section 100307, which broadly requires that CIRM-funded inventions must be made available for research purposes at no cost.
- Clarify, narrow or remove "failure to keep the licensed invention available to the public for research purposes" as grounds for termination of licenses included in Section 100306(f).

We look forward to working with the ICOC as it finalizes this policy, and we would be happy to further discuss these comments in additional detail.

Thank you for your attention to this important matter.

Sincerely,



David L. Gollaher, Ph.D.
President and CEO
California Healthcare Institute

cc: Mary E. Maxon, Ph.D.

Ref. 3

Scott Tocher

From: Vail, Shelby [Shelby.Vail@asm.ca.gov]
Sent: Thursday, June 15, 2006 3:41 PM
To: CIRM Nonprofit IP Regs Comments
Subject: DRAFT CIRMletter_1.DOC

June 8, 2006

VIA E-MAIL NONPROFITIPREGS@CIRM.CA.GOV
FOLLOWED BY U.S. MAIL

C. Scott Tocher, Interim Counsel
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Re: Comments on Proposed Regulations – Intellectual Property Policy for Non-Profit Organizations (IPPNO)

Dear Sirs:

I welcome this opportunity to comment on the California Institute for Regenerative Medicine's (CIRM) interim regulations addressing Intellectual Property Policy for Non-Profit Organizations (IPPNO) as approved by the Independent Citizens' Oversight Committee (ICOC) on February 10, 2006. In my district, I represent a broad segment of the state's biomedical sector including some of California's leading life sciences companies, universities, and academic research institutions.

California's highly-regarded life sciences infrastructure -- basic science, venture capital, commercial life sciences companies, and the many support services (e.g. legal, accounting, architectural) essential to transforming scientific discoveries into products -- is the reason our state is the global leader in biotechnology. Public funding of stem cell research in California can exert enormous influence, as can the policy choices related to funding decisions.

I am concerned that a provision in the Intellectual Property Policy for Non-Profit Organizations (IPPNO), would appear to block the commercialization of any CIRM-supported invention that is used primarily in research. As a result of this provision, CIRM-funded research tool IP, is likely to either languish on university shelves or be distributed, at best, on a limited (and un-enhanced) basis through informal networks of researchers. Under the existing provision, no private funds will be devoted to improving or distributing any CIRM-funded research-related inventions.

7/7/2006

I write to suggest that the IPPNPO research use provision be eliminated or modified so that these traditional economic forces can be used to support the objectives of Prop 71 in the area of research tools.

What are research tools and why should they matter to the ICOC?

In the life sciences, research tools are typically defined as the full range of products and systems that have their primary usefulness in research or discovery rather than as an FDA-approved product or an integral component of an FDA-approved product. They include but are not limited to bioinformatics, animal disease models, cell lines, cell culture and media, reagents and assays, antibodies, clones and cloning tool methods, cDNAs; expressed sequence tags (ESTs), full-length genes and their expression products; as well as methods and instrumentation for the sequencing of genomes, quantification of nucleic acid molecules, detection of single nucleotide polymorphisms (SNPs), and genetic modifications.

Many research tools are patented. Indeed, in 2005, the National Institutes for Health (NIH) published guidance encouraging NIH funding recipients to patent tools "when it is clear that private sector investment will be necessary to develop and make the invention widely available."

Patented research tools have had a significant impact on the biotechnology and drug discovery fields, and significant changes in IP controls underlying research tool innovation and commercialization, as contemplated by the CIRM, may affect drug development and patients.

The IPPNPO research use provision and its effects on research tools and drug discovery

The IPPNPO represents recognition of the importance of research tools. However, they are so important, the policy concludes that any CIRM-funded IP that has utility in research must be made available to any California researcher at no cost. The research use provision reads:

"Grantee organizations agree that California research institutions may use their CIRM-funded patented inventions for research purposes at no cost. Grantee organizations shall require the same agreement of each of their licensees of CIRM-funded patented inventions."

The problem with this approach is that inventions that must be made available at no cost

by definition can't be commercialized. No private firm will license a research -related invention that cannot be protected in a research environment and must be made available to all California researchers for free. No private funding will be used to enhance that invention and none of the energy of the commercial market will be made available to manufacture, advertise, or disseminate it.

I'm concerned that the net effect could be that CIRM-funded research-related inventions will be less readily available, and will be improved at a slower pace than inventions invented without CIRM support and slower than they would if the CIRM removed the requirement that all its IP be freely available to California researchers. Ultimately, the delay in research invention development will delay the pace of therapies and cures development.

What problem is being addressed and/or resolved?

Given (1) that a good deal of drug development and device-related research in the U.S. is covered by an infringement exception, (2) that all non-commercial research is already covered by an existing research use exemption, (3) that other provisions in law allow research funders to ensure the availability of key IP for research, **and** (4) that commercial licenses are generally available to researchers to enable “authorized use” of inventions, why is an additional, radical research use provision required in the IPPNPO?

Several members of the CIRM stakeholder community sometimes point to a specific case in which an important research tool has not been made as readily available as the research community would like. It's not my contention that the current system is perfect, but rather that it works well almost all the time. To address the occasional problem, we should not undermine a productive and effective patent system that has enabled the fastest and most significant advances in medical research and healthcare treatment in human history. This is especially true given that alternative remedies to the few problem cases already exist. It could be that the IPPNPO proposal undermines a system effective 99% of the time in order to solve a problem that arise perhaps 1% of the time.

Academic researchers have concluded research access to IP is not an issue. Recent academic studies have examined exactly the question at issue here: Are biomedical researchers hampered by patents and IP licensing requirements? The answer, according to the leading recent studies, is no.

The essence of both a 2003 and 2005 interview and survey studies – “...access to patents on knowledge inputs rarely imposes a significant burden on academic biomedical research.” [J.P. Walsh, the W.M. Cohen, A. Arora, Science 299, 1021 (2003); Walsh, Cho, and Cohen, September 2005]

Request and Recommendation

For all the reasons outlined above, I respectfully request and recommend that the ICOC remove the current research use provision. Current research use law and practice, combined with IP dissemination guidelines akin to those in use at NIH would meet Prop 71's objectives far better than the current Research Use provision in the IPPNPO.

Alternatively, should the ICOC conclude that some provision is necessary, it is vital that it adhere to three basic principles:

1. Do no harm to the academia-industry research tools partnership that is currently working well nearly all the time -- to the benefit of researchers and patients
2. Focus on the goal of broad access for California researchers to CIRM funded IP, not the means.
3. Preserve the opportunity for the commercial sector to support the CIRM mission and goals in the research tools domain, as the agency has worked to do in therapeutics and devices.

Sincerely,

7/7/2006

Shirley A. Horton

SAH:sv

cc: Kirk Kleinschmidt

Director of Legislation and Research Policy

California Institute for Regenerative Medicine

227615.1

7/7/2006

COMMENTS OF THE
BIOTECHNOLOGY INDUSTRY ORGANIZATION
ON
CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE'S
NOTICE OF PROPOSED REGULATION ADOPTION
CALIFORNIAN CODE OF REGULATIONS
TITLE 17.—PUBLIC HEALTH
PROPOSED REGULATIONS: INTELLECTUAL PROPERTY POLICY
FOR NON-PROFIT ORGANIZATIONS

JUNE 19, 2006
NONPROFITIPREGS@CIRM.CA.GOV

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June 16, 2006

BY ELECTRONIC MAIL TO NONPROFITPREGS@CIRM.CA.GOV

Mr. C. Scott Tocher
Interim Counsel
California Institute for Regenerative Medicine
250 King Street
San Francisco, CA 94107

**Comments on Proposed Regulation: Adoption of Californian Code of
Regulations, Title 17.—Public Health, Proposed Regulations:
Intellectual Property Policy for Non-Profit Organizations**

Dear Mr. Tocher:

The biotechnology industry is one of the most research and development intensive and capital-focused industries in the world. It is the bedrock for the entire world of biomedical research. In 2003, the U.S. biotech industry spent \$17.9 billion on research and development and put into the hands of the public more than 300 biotech drug products and vaccines and hundreds of medical diagnostic tests. This, despite the decades-long development time and the complex regulatory process the industry must face before bringing its products to market. The U.S. system of commercializing scientific discoveries—the funding of basic research, transferring technology from the academic sector, taking advantage of the availability of risk capital, and leveraging the fact that investors are willing to take risks—has paid off. The United States currently leads the world in the area of biotechnology because strong patent laws and flexible technology transfer systems have provided favorable incentives to mitigate the high risks.

At the federal level, rapid commercialization of scientific discovery did not fully come about until the enactment of the Bayh-Dole Act in 1980. Prior to enactment of this legislation, publicly funded research was owned by the government and offered for licensing on a non-exclusive basis or simply

dedicated to the public. There was little incentive for businesses to undertake the financial risk to develop a product. The result was that only 5% of publicly funded discoveries were ever developed into new or improved products.ⁱ The Bayh-Dole Act allowed universities and research institutions to patent and retain title to their inventions. Moreover, the Act allowed for flexibility in licensing of publicly funded inventions. The motivation to license the technology in expectation of royalty payments was created. This provided a necessary impetus for the transfer of publicly-sponsored research to the private sector, thereby dramatically stimulating the commercialization of federal government-supported research. The result among other things is the existence of innovative new therapeutics, diagnostics and tools, industrial processes and agricultural products for the benefit of society.

The California Institute for Regenerative Medicine (CIRM), in its stewardship of the public funds dedicated to stem cell research, has proposed policies that are antithetical to the federally tested system of technology transfer created through the Bayh-Dole Act. Although the CIRM draft IP policies are often described as going “beyond” Bayh-Dole these policies, if implemented, would actually take California backward to the pre-Bayh-Dole era when few promising publicly funded technologies ever reached the hands of the public.

BIO AND THE BIOTECHNOLOGY INDUSTRY

The Biotechnology Industry Organization (BIO) is a trade association of more than 1,100 companies, universities, research institutions, and affiliated organizations worldwide. BIO members are engaged in biotechnology research on medicines, diagnostics, agriculture, and environmental and industrial applications. BIO represents an industry that has already provided more than 300 million people with benefits from more than 250 commercially approved drugs, biologics and vaccines.^{ii/} Over 20 percent of BIO’s membership resides in the state of California—the birthplace of biotechnology. BIO’s members, the majority of whom are involved in the development of healthcare related products and services, have a long history of focusing their efforts on intractable diseases including various cancers, AIDS, Alzheimer’s disease, heart disease, diabetes, multiple sclerosis and arthritis. In addition, biotechnology companies and researchers are responsible for the development of hundreds of medical diagnostic tests, many biotechnology-derived foods, environmental products and other industrial products.^{iii/}

In California over 1200 "spin-off" companies have been established over the years through the effects of Bayh-Dole from Stanford, and this is just one example. Successful "spin-off" ventures help bring valuable products to market, and also develop the vibrant Silicon Valley which leads in high tech, biotech, and medical device industries. This thriving business ecosystem, in turn enables further R&D initiatives and two-way technology flow between academia and industry.

CIRM'S IP POLICIES

BIO supports the goals of the California Stem Cell Research and Cures Act (Prop 71) which is designed to fund stem cell research as well as other opportunities for the development of regenerative medical diagnostics, treatments and therapies. The potential for the development of innovative products and technologies in California as a result of its stem cell initiative is extraordinary. The existence of the infrastructure necessary to realize the promise of stem cell research in California – in the form of unsurpassed research institutions and intellectual capital as well as a robust venture capital and commercial development community – further enhances the chances that successful cures, therapies, diagnostics, and tools will result from the CIRM's efforts. But as we have learned too well in the federal setting prior to the enactment of the Bayh-Dole Act, an infrastructure without an environment and framework conducive to commercialization will only generate promising research that will languish on the shelves of California's pre-eminent research institutions for years to come. Further, without financial incentives, industry is unlikely to license technologies developed by Universities with CIRM funds, which will result in the loss of additional funding for further research and development in this critical area.

There are two major components of the proposed intellectual property policies for non-profit organizations (IPPNPO) which reduce the likelihood that CIRM-funded discoveries will reach patients and other end users. These concerns are also salient to intellectual property policies in general.

First, the proposed policy mandates that grantee organizations exclusively license CIRM-funded patented inventions only to organizations that plan to provide access of resultant products to uninsured California patients. The policy further mandates that the licensees agree to provide any resulting therapies that will be purchased by California public funds at a cost not to exceed the federal Medicaid price. These proposed licensing restrictions restrain free markets by imposing a de facto price control over the resulting

product. In its proposal, CIRM recognizes that economic incentives will be necessary to enable commercial development.^{iv} However, the requirement to only grant exclusive licenses to organizations with plans to provide resultant products at Medicaid prices in effect reduces incentives for companies to commercialize such products.

Drug development in the biopharmaceutical industry is a very high risk endeavor. A study has shown that pharmaceutical companies spend an average of \$800 million and 10-14 years to develop a single pharmaceutical product^v. Companies will only invest in such high risk endeavors if there is a potential to recoup the development cost. At the same time, the vast majority of BIO's members are start-ups that currently have no products on the market. Rather they rely on their patent assets to generate R&D financing from the private sector. For example, in 2002, only approximately 1.6 percent of the industry's R&D funding originated from government sources; the remaining 98.4% came from private sector financing. In many instances these patent assets are licensed far upstream in the development time-line, making it difficult for either a company or its investors to know what pricing and access regimes will be viable. Without flexibility in product pricing and structure of license arrangements, the ability to secure private funding to support the development of innovative stem cell products would be severely hindered.

A second area of concern in the IPPNPO is the research use exemption provision. This provision requires that CIRM funded inventions be provided to all "California research institutions" "for research purposes" "at no cost".

Research tools are core enabling technologies for future stem cell research. Currently, many companies license research tool IP from universities, enhance it, and commercialize the resulting products. Most of these products are then made widely available to the research community through websites, catalogues, in house supply centers, and the like. The benefit to the research community is enhanced biological understanding and faster, simpler, and more repeatable tools and techniques of experimentation. In research tools, as in therapeutics, the opportunity to patent and to commercialize a product is a powerful incentive for innovation.

The IPPNPO provision interrupts this well functioning system by requiring that all CIRM funded IP be made available to all California researchers at no cost. This requirement greatly reduces the incentive for a company to commercialize a CIRM funded research tool, since the California research

market must be served at no cost. As a result, promising CIRM funded research tools are likely to remain on the shelf, undeveloped, as was so often the case in the pre Bayh Dole era at the NIH.

These provisions substantially reduce or eliminate the incentives to commercialize patented stem cell-related technologies and products even in spite of the generous funding provided by Proposition 71. The opportunity for firms to take the inventions supported by Prop 71, and further invest their own money and efforts into creating innovative tools, technologies and products for chronic diseases will be negated by strict obligations and inflexible licensing schemes proposed by the CIRM.

CONCLUSION

BIO urges CIRM to carefully reconsider these issues in the formation of any policies. Failure to do so would likely have significant undesirable consequences on CIRM's ability to achieve its goals. For example, during the 1990's two issues similar to those presented by CIRM's proposed policies arose out of public policy initiatives. Concerns that health care reform proposals from the early 1990's could lead to price controls led to perturbations in the market for biotechnology investment. The impact potential price controls on the biotechnology industry was immediate and powerful. The capital markets crashed and investment nearly dried up.

A similar result occurred in 1999 when President Clinton and Prime Minister Blair were cited in the press as supporting the notion that certain classes of patented genetic information should be freely available to all at the time the human genome was "unraveled." Despite a clear correction by the President the next day, it took six months for the biotechnology capital markets to recover.

In both cases, a threat to free-market protection of intellectual property drove investors away from biotechnology and research. The Bayh-Dole Act was designed to facilitate the transfer of publicly funded research to the private sector for further development and commercialization. The careful balance set forth in the act has been hugely successful. The impact of the Act is evident today in the over 1400 biotechnology companies in the United States and hundreds of biotechnology products in the marketplace.

We have learned from history that attempts to control prices or restrict flexibility in licensing are likely to disincentivize biotechnology companies

from undertaking the huge risks to bring innovative products and services to all Americans.

BIO urges CIRM to reconsider its proposed IP policy and look to the Bayh-Dole Act as an overwhelmingly successful example of a framework that has achieved goals similar to that of CIRMs'.

Sincerely,

A handwritten signature in black ink, reading "James Greenwood". The signature is fluid and cursive, with the first name "James" and last name "Greenwood" clearly legible.

James C. Greenwood

President & CEO

Biotechnology Industry Organization

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i Association for University Technology Managers, Annual Report, 2003

ii/ Facts about the biotechnology industry are derived from data compiled by (BIO) at www.bio.org/er/statistics.asp.

iii/ Kenneth I. Shine, President, Institute of Medicine, "Welcome," in National Research Council, *Serving Science and Society in the New Millennium*. Washington, D.C.: Nat'l Academy Press, 1998. (proclaiming that, whereas "the 20th century will be known as the century of physics and astronomy ... [b]ut the 21st century will be the century of the life sciences in all their ramifications.").

iv/ Section 100306, lines 9-15 of CIRM Proposal.

v <http://csdd.tufts.edu/NewsEvents/RecentNews.asp?newsid=29>, May 13, 2003, Press Release.

Ref. 5

Scott Tocher

From: Ben Crow [bencrow@ucsc.edu]
Sent: Friday, June 16, 2006 11:48 AM
To: CIRM Nonprofit IP Regs Comments; Mary Maxon
Cc: Pitts, Lawrence
Subject: CIRM Nonprofit Intellectual Property Policy - Comments
Attachments: CIRM-IP-policy-UCcomments.doc

To: CIRM;
CIRM Independent Citizen's Oversight Committee;
ICOC Intellectual Property Task Force Subcommittee

From:

University of California Academic Council Special Committee on Scholarly
Communication (SCSC);

Professor Lawrence Pitts, Chair

(conveyed by SCSC member Ben Crow)

Re: CIRM Intellectual Property Policy regarding publication of
CIRM-sponsored research: fostering scientific progress through open
access

We applaud the CIRM draft policy statement that "data, knowledge, (and) scientific articles will be shared broadly and promptly," but we believe that the current regulation draft that requires only a short abstract be made available to the public is far too incomplete to meet that principle or CIRM's and the public's needs. Our committee and the University of California Academic Council believe that a requirement that publications resulting from CIRM-funded research be placed in an open-access repository will much better meet these needs.

Attached to this email is a document that fully presents our concerns and offers draft policy language that would address them. We would be pleased to answer any questions you have and hope to have a representative at the Task Force discussion of comments, which we understand to be scheduled for July 14, 2006 in Sacramento. Thank you for your consideration of these comments.

Ben Crow
for Prof Lawrence Pitts
Chair, UC Academic Council Special Committee on Scholarly Communication.

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Ben Crow, Associate Professor, Sociology, University of California, Santa Cruz.

7/7/2006

Phones: 831 459 5503 (W); 650 245 6769 (Mobile); (831) 421 0928 (H).

Website: <http://sociology.ucsc.edu/directory/details.php?id=4>

Atlas: <http://ucatlus.ucsc.edu/>

Date: June 16, 2006

To: CIRM; CIRM Independent Citizen's Oversight Committee; ICOC Intellectual Property Task Force Subcommittee

From: University of California Academic Council Special Committee on Scholarly Communication (SCSC); Professor Lawrence Pitts, Chair (conveyed by SCSC member Ben Crow)

Re: CIRM Intellectual Property Policy regarding publication of CIRM-sponsored research: fostering scientific progress through open access

We applaud the CIRM draft policy statement that "data, knowledge, (and) scientific articles will be shared broadly and promptly,"¹ but we believe that the current regulation draft that requires only a short abstract be made available to the public is far too incomplete to meet that principle or CIRM's and the public's needs. SCSC and the University of California Academic Council believe that a requirement that publications resulting from CIRM-funded research be placed in an open-access repository will much better meet these needs. This is the policy that was forwarded to the ICOC by University of California President Robert Dynes in May 2005, appended here.²

The "Publication requirements" (Section II, H(a.)) in the current draft regulations are **not**, in fact, "structured to extend the sharing of CIRM-funded intellectual property beyond practices commonly in use by the scientific community" as claimed in Section II, K(2). In contemporary scholarly publishing abstracts of published work are usually readily and openly available. While abstracts do aid the search for the existence of relevant material, by themselves the abstracts are of very limited value for follow-on research compared to the full publications. Making abstracts available does little to remove the barriers to access when publicly-funded research results are available only through subscription-based and often high-priced journals.

In fact, we believe the current CIRM publication policy draft fails to meet the intent of the principle of broad sharing on a number of points:

- It requires deposit and open access to an abstract rather than the research publications and data themselves, on which further scientific progress and public knowledge depend (Section II, H(a.1.);
- It places the burden of access to the full research publication on a request between a potential reader and the author(s) (Sections II, H(a.3); II, H(b.1)), an approach which is inefficient and difficult to scale to the potential large size of the interested audience and which imposes unnecessary burdens and delays on both the author and reader;
- It proposes an incomplete and redundant and perhaps expensive central repository solution – construction of a CIRM Electronic Library Repository (CERL - Section III, L(a.ii)) – which would unnecessarily constrain the archiving and long-term management of research

¹ CIRM Intellectual Property Policy For Non-Profit Organizations. Section III, K(2). *Intellectual Property, including but not limited to data, knowledge, scientific articles, biomedical materials and patented inventions, that are made in the performance of CIRM-funded research will be shared broadly and promptly with the scientific community. This CIRM sharing policy is structured to extend the sharing of CIRM-funded intellectual property beyond practices commonly in use by the scientific community in 2005.*

² Also available at <http://www.universityofcalifornia.edu/senate/reports/rcd.2.klein.icoc.cirm.0505.pdf>

results by requiring the CERL to contain only the abstracts mentioned above (and “biographical sketches”) rather than full content; and create potentially redundant capacity given the presence of publicly operated trusted open access repositories such as PubMed Central³ and UC’s eScholarship Repository.⁴

- It seems inappropriately to imply that the policy grants post-publication permission for an author to deposit research publications into a trusted repository (Section III,L(a.iii), when such permission is actually and entirely dependent on the author’s contract with a publisher. Such deposit, as outlined in the UC Academic Council proposal, is only likely to be effective and ubiquitous when it is a condition of the grant award, establishing, in effect, a pre-existing CIRM use license for publicly-funded research results.
- Finally, it ignores developments which confirm the importance of open access to publicly funded research and, by not being assertive in this regard, denies California’s researchers, its public, and the CIRM itself the opportunity to create positive change.

The rapidly changing environment of scholarly publishing includes escalating support for and pressure toward open-access to publicly funded research. We believe that the CIRM publications policy should be on the forefront of such developments. Such developments include our own proposal, adopted on May 10, 2006 by UC’s Academic Assembly, which calls for UC President Dynes to establish a group to formulate a change in UC copyright policy whereby UC faculty grant a license to the UC Regents to place a copy of the faculty’s scholarly work in an open access repository. The policy would encourage faculty to license only to publishers an exclusive first commercial publication right. Recognizing that occasionally a faculty member might feel it important that his or her work be published in a journal or conference proceedings whose publisher won’t allow the granting of such a license, UC’s proposed policy will allow the possibility of an opt-out for single articles. But in recommending that exceptions go through an opt-out process and by endorsing the principle of a default transfer of a license for open access deposit, it is clear that the UC faculty wishes to ensure the widest possible dissemination of their work via its availability in well-managed, online publicly open sites.

Other important developments which overtake the draft CIRM policy include in just the last few months: proposed legislation mandating open access to publications resulting from nearly all federally funded research (the Federal Research Public Access Act – see below), a proposal for the NIH to strengthen its open access policy from voluntary to required deposit of NIH-funded research results into PubMed Central; rapid movement in the UK and elsewhere in Europe and Australia toward open access to publicly funded research results; growing evidence that open access does, in fact, lead to greater and more timely impact; substantial evidence that researchers are willing to follow a funder’s requirement to provide open access to results; and copyright tools, such as author’s pre-written addendums to publication agreements, that facilitate and standardize the distribution of copyright rights. Further information on these developments is attached to these comments.

To facilitate your consideration of an effective open access and archiving policy the SCSC proposes, consistent with actions taken by the UC Academic Council and the Academic

³ The National Library of Medicine’s PubMed Central (<http://www.pubmedcentral.nih.gov/>)

⁴ The University of California’s eScholarship Repository (<http://repositories.cdlib.org/escholarship/>)

Assembly, the following changes to the CIRM publication draft regulations, requiring open access deposit of CIRM-funded research results within six months of publication.

It is important to note that this suggested policy change need not disadvantage junior or untenured researchers who are under pressure to publish in certain journals regardless of the copyright policies of the journal publisher. Within the spirit of the proposed UC policy mentioned above, exceptions to extend the delay before open access deposit could be granted when it is clear that open-access deposit would jeopardize a researcher's ability to publish with a journal. It is also important to note that both well-established (e.g. *Nature*) and new highly prestigious journals (e.g. *PLoS Medicine*) and non-traditional publishing venues with liberal copyright policies are increasingly available. In addition, the SCSC believes, and has stated in one of its whitepapers⁵ the need for university peer review processes to evaluate the quality of research appearing in **all** venues to ensure both the quality of the venue/publication as well as the quality of the research.

H. Sharing of CIRM-Funded Intellectual Property:

a. Publication requirements

1. Within 60 days of the publication of CIRM-supported research results in a scientific journal, PIs must submit to CIRM a 500 word abstract written for the general public that highlights the findings of the published body of work. In addition, PIs must submit a biographical sketch to accompany the abstract. The abstract and the biographical sketch will be deposited into the publicly-accessible CEDR, to be accessed via the CIRM website.
- 1a. *(NEW LANGUAGE) Within 6 months of publication of CIRM-supported research results in a scholarly journal or conference proceedings, PIs must place the scholarly work in a trusted non-commercial open-access online repository. This will require that the PI either a) retain copyright and license to a publisher only the right of first commercial publication or b) retain a license for this purpose if he/she transfers copyright for the scholarly work to a publisher. If the publisher refuses to allow the retention of such a license, the PI may apply to CIRM for a one-time exception to the requirement in the form of either a) a waiver of the requirement, or, preferably, b) an extension of the delay of open-access deposit of the work from 6 to 12 months.*
2. One copy of each publication resulting from work performed under a CIRM grant must accompany the mandatory annual progress report submitted to CIRM.
3. In the final manuscript, authors must include the URL of a website where the CIRM MTA (or similar document) can be accessed to facilitate requests for publication-related materials.
4. CIRM grantees must acknowledge CIRM support of research findings in publications, announcements, presentations, and press releases by the grantees. An acknowledgement should be to the effect that:

⁵ Evaluation of Publications in Academic Personnel Processes at <http://www.universityofcalifornia.edu/senate/committees/scsc/cap.eval.scsc0506.pdf>

“The research was made possible by a grant from the California Institute for Regenerative Medicine (Grant Number _____). The contents of this publication are solely the responsibility of the authors and do not necessarily represent the official views of CIRM or any other agency of the State of California.”

b. Publication-related biomedical materials requirements

1. Grantees shall share biomedical materials described in published scientific articles for research purposes in California within 60 days of receipt of a request and without bias as to the affiliation of the requestor unless legally precluded. Under special circumstances, exceptions to the above are possible with approval by CIRM. Alternatively, authors may provide requestors with information on how to reconstruct or obtain the material. Materials are to be shared without cost or at cost.

DRAFT

**THE CALIFORNIA STEM CELL RESEARCH AND CURES BOND ACT OF 2004
DRAFT POLICY ON PUBLIC ACCESS AND ARCHIVING OF RESEARCH RESULTS**

**PROPOSED BY THE ACADEMIC COUNCIL SPECIAL COMMITTEE ON SCHOLARLY COMMUNICATION
ADOPTED BY THE ACADEMIC COUNCIL ON
March 22, 2005**

The California Stem Cell Research and Cures Act declares an urgent need for stem cell “research and facilities” to treat and cure diseases and injuries and whose results will “benefit the California economy” and “advance the biotech industry in California.” The act also requires “strict fiscal and public accountability.”

Goals: Public access and research archiving

In support of these declarations, the following draft policy on public access and archiving of research results is submitted to the California Institute for Regenerative Medicine (CIRM) and its Independent Citizen’s Oversight Committee (ICOC) for their consideration. If adopted, this policy will meet several important goals:

- **Accelerate research progress and provide California’s public access** without cost to a collection of published results of taxpayer and Act-funded research.
- **Create a stable and permanent California-based archive** of peer-reviewed research publications and source data to ensure the permanent preservation of these vital research findings.
- **Secure a searchable collection of peer-reviewed research publications** that the Institute and the ICOC can use to manage its research portfolio and measure scientific productivity and progress.

The policy establishes an online open-access research repository configured so that:

- Scientific information arising from Act-funded research is available without fee and in a timely fashion to other scientists, health care providers, medical and other students, teachers, and the California citizens who fund the research;
- The critical roles of journals and publishers in peer review, editing, and scientific quality control processes are preserved;
- Deposit in the repository supplements but does not replace traditional publication, providing access to those who cannot afford journal subscription costs, after an author-defined delay of no more than 6 months;
- Where appropriate and at the researcher’s discretion, source data also can be deposited and results are linked to such data;
- Formal technology transfer through patents, etc. remains intact, just as it does through the current system of publishing peer-reviewed research findings.

Similar public access policies are under development or recently adopted by the NIH⁶, the UK research councils⁷, and the Wellcome Trust⁸, among others. While similar in intent, they differ in the particulars, especially with regard to: 1) the mandate: requiring vs. encouraging public access; 2) the delay: immediate public access or a delay of 6 or 12 months to accommodate concerns about preserving the market for journals; and 3) the timing: deposit and public access coordinated with the finalization of the peer review process or with initial publication.

⁶ “Policy on Enhancing Public Access to Archived Publications Resulting from NIH-funded Research” (<http://grants.nih.gov/grants/guide/notice-files/NOT-OD-05-022.html>).

⁷ “House of Commons, Science and Technology, Tenth Report.” (<http://www.publications.parliament.uk/pa/cm200304/cmselect/cmsctech/399/39903.htm>)

⁸ “Research Publishing and Open Access.” (<http://www.wellcome.ac.uk/node3302.html>)

The Proposed Policy⁹

Beginning [DATE], CIRM-funded investigators are required to submit to a trusted publicly-accessible repository¹⁰ an electronic version of the author's final manuscript resulting from research supported, in whole or in part, with direct costs from CIRM. The author's final manuscript is defined as the final version that has been accepted for journal publication, and includes all modifications from the publishing peer review process. Authors also are encouraged to submit source data upon which the published results are based, as well as book chapters, editorials, reviews, or conference proceedings related to the work.

Under this Policy, electronic submission is made directly to a trusted, publicly accessible online repository, either at the investigator's or another institution. (One example is the University of California's *eScholarship Repository*¹¹, which is hosted by the University of California's California Digital Library¹² and is a publicly-accessible, stable, permanent, and searchable electronic archive of research data and results.) At the time of submission to the repository, the author will state when his or her final manuscript should be made publicly accessible¹³. Posting for public accessibility is required within 6 months of acceptance for publication and is strongly encouraged to occur immediately upon acceptance of a final manuscript. Deposited material will clearly note the publication in which it first appears.

If it is in possession of the appropriate copyrights, the publisher may choose to furnish the repository with the publisher's final version, which, when made publicly accessible, will supersede the author's final version. The publisher may provide or allow public access to the publisher's final version sooner than six months from acceptance of the manuscript's final version.

This Policy can provide the means for CIRM-supported investigators to fulfill any requirement to provide publications as part of research progress reports.

By creating a repository service for public access to peer-reviewed CIRM-funded research, the CIRM, its funded researchers and participating institutions are assisting scientists, educators, and health care providers to more readily exchange research results and the public to have greater access to regenerative medicine-related research publications. Such a repository could become a central resource for stem cell research publications and data resulting from CIRM and other research worldwide, benefiting Californians and the interested public everywhere.

⁹ This policy borrows and benefits from the creation during 2004-2005 of the NIH's "Policy on Enhancing Public Access to Archived Publications Resulting from NIH-funded Research" (<http://grants.nih.gov/grants/guide/notice-files/NOT-OD-05-022.html>). While differing in particulars it is similar in stated intent.

¹⁰ A trusted publicly-accessible California repository is one that provides reliable, long-term access to managed digital resources and is internet-accessible, operated by a California-based institution with explicit preservation and governance policies, uses data formats and technology management that conform to industry standards, and is interoperable with other repositories.

¹¹ <http://repositories.cdlib.org/escholarship/>

¹² <http://www.cdlib.org/>

¹³ For these purposes it is presumed that the author has retained the necessary copyrights in his or her publication agreement with the publisher, or has verified that the publisher's copyright policy permits this action.

Open Access Developments June 2005 – June 2006

“..biomedical science simply can't function efficiently any more without open, unrestricted access to research results....[W]e have seen from our experience with the genome how important it is that the data is free and that everyone can access it. What this means is that we have to completely re-think the way science reports its findings.” Vitek Tracz, Founder of BioMed Central in an interview By Richard Poynder. May 23. 2006.
<http://poynder.blogspot.com/2006/05/interview-with-vitek-tracz.html>

The following developments show a wide cross-section of the public, legislators, and researchers expressing the need for or taking actions “to expand the public’s access to research . . . (a)nd . . . accelerate scientific innovation and discovery,” principles that CIRM has espoused but which its draft IP policy fails to meet.

- **Federal Research Public Access Act.** May 2, 2006. Senators John Cornyn (R-TX) and Joe Lieberman (D-CT) introduced the Federal Research Public Access Act of 2006 (FRPAA) in the US Senate. The bill requires every federal agency with an annual research budget of more than \$100 million - including NASA, the EPA, NSF, and the Departments of Agriculture, Commerce, Defense, Education, Energy, Health and Human Services, Homeland Security, and Transportation - to implement a policy for public access to research results, providing such access no more than 6 months after publication. http://cornyn.senate.gov/doc/archive/05-02-2006_COE06461_xml.pdf
- **NSB Report on Open Exchange of Data.** June 6, 2006. The National Science Board reported that the U.S. government risks jeopardizing the “quality and credibility” of Federally sponsored scientific research by failing to encourage the open exchange of scientific information, and went on to recommend that the administration establish a consistent policy for exchange of government research. <http://www.nsf.gov/nsb/>
- **NIH Mandate.** June 2006. In the Appropriations Bill for fiscal 2007, the U.S. House Appropriations Committee explicitly directs the NIH to institute mandatory, six-month public-access to agency-funded work. The NIH’s current policy in this area was issued in May 2005 and calls for voluntary posting on PubMed Central within a year of publication. The Appropriations Committee action follows the April 10, 2006 NIH Public Access Working Group’s reaffirmation of its November 2005 recommendation that all NIH-funded research be made publicly available via PubMed Central no later than six months after publication, and an endorsement of that recommendation by the NIH Board of Regents. Several groups, such as the Alliance for Taxpayer Access (ATA), the American Cancer Society, and the *New England Journal of Medicine*, have expressed their support for a mandatory policy with a six-month posting deadline. <http://publicaccess.nih.gov/>
- **Public Support for Open Access.** May 31. 2006. In an online survey of public attitudes conducted recently and released today by Harris Interactive®, 8 out of 10 (82%) adults polled said they believe that “if tax dollars pay for scientific research, people should have free access to the results of the research on the Internet.” <http://www.taxpayeraccess.org/media/Release06-0531.html>
- **Author’s Acceptance of Open Access Mandates.** June, 2005. A large study found that 81% of researchers would willingly comply with a mandate from their employer or research funder to deposit copies of their articles in an open access repository. Swan, A. and Brown, S. (2005) Open

access self-archiving: An author study. Technical Report, External Collaborators, Key Perspectives Inc. <http://eprints.ecs.soton.ac.uk/10999/>

- **The American Center for CURES Act.** December 7, 2005. S.2104; introduced by Senator Joe Lieberman in December 2005), would mandate OA to the bulk of federally-funded medical research. CURES Act, summary, December 7, 2005
<http://lieberman.senate.gov/documents/bills/051207curesbill.pdf>.
- **Aligning Copyright with open access.** June 6, 2006. A major effort of the Science Commons project (itself a component of the Creative Commons project) launched the Scholar's Copyright Project whose declared aim is to provide standard, responsible copyright agreements ensuring the right of scholars to archive their work on the public Internet.
http://sciencecommons.org/literature/scholars_copyright
- **UK Open Access policies.** The Research Councils UK (RCUK) – the UK's largest public funding agency - is considering a policy that would mandate open access to the publications resulting from research it funds. RCUK, Access to Research Outputs <http://www.rcuk.ac.uk/access/index.asp>
Also, the UK's largest private medical science funder, the Wellcome Trust, has mandated open access to research publications resulting from their grants (http://www.wellcome.ac.uk/doc_wtd002766.html). Within that policy they also provide grant funding to cover any publication charges levied by a journal that result in open access to the article. We applaud CIRM's similar decision to support publication charges (Section III,L(a.i.)), but, as detailed in the body of these comments, suggest that the current CIRM policy provisions do not, in fact, credibly manifest the "broad sharing" principle.
- **Open access impact advantage.** Using various targets and analytical techniques, a steady stream of research studies confirm the increased citations and readership of articles that are made openly available (<http://opcit.eprints.org/oacitation-biblio.html>). The most recent study examined 1492 articles published during one 6-month period in the Proceedings of the National Academy of Science (Eysenbach. 2006. <http://dx.doi.org/10.1371/journal.pbio.0040157>)



June 16, 2006

C. Scott Tocher, Interim Counsel
Members of the Independent Citizen's Oversight Committee
California Institute For Regenerative Medicine
210 King Street
San Francisco, CA 94107

Dear Mr. Tocher and Members of the Committee:

BIOCOM leads the advocacy efforts of the Southern California life science community, with more than 460 members including biotechnology and medical device companies, universities, basic research institutions, and service support firms. We would like to voice our concern with portions of the Intellectual Property Policy for Non-Profit Organizations (IPPNPO) before the final document is ratified.

Section II H e states, "*Grantee organizations agree that California research institutions may use their CIRM-funded patented inventions for research purposes at no cost. Grantee organizations shall ensure that such use is preserved in their licenses of CIRM-funded patented inventions.*" This proposed provision is likely to dissuade companies from participating in collaborations and partnerships with CIRM-funded researchers..

BIOCOM recognizes the importance of access to information and the benefit of shared information in academic and research settings. But the citizens of California approved Proposition 71 with the belief it would lead to innovative cures, a process that necessarily involves private industry. By definition, the primary value of many life science companies is inextricably intertwined with the value of its patents. To refer to one of the arguments put forward in the ballot argument in favor of Proposition 71,

"By making California a leader in stem cell research and giving our State an opportunity to share in royalties from the research, 71 will generate thousands of new jobs and millions in new state revenues..."

This is recognition that CIRM policies should not simply advance research, but do so based on the expectation that at least some of that research will result in marketable therapies. As many researchers are focused primarily on publication, entrepreneurial competition, properly fostered and governed, will better accomplish the goal of helping to speed life-changing therapies to market.

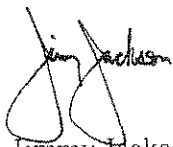
A driving force of the biotechnology revolution has been the willingness of investors to risk significant amounts of capital knowing that relatively few products will ever see the market. Current statistics indicate that only 8% of therapeutics which start FDA Phase I clinical trial testing are eventually approved for general distribution. If the final IPPNPO significantly reduces the ability of venture capitalists and investors to mitigate their risk through licensing and royalty potential – as it does in the provisions cited above -- they will pursue other options. The primary result will be reduced impact for CIRM funded discoveries, both in research advancement and in new treatments.

Further, this provision is overly broad; it appears possible a research institution may use a patented invention to develop a successor therapy, and then partner into a technology transfer agreement from which the research institution will benefit monetarily. Meanwhile, the company which invested great amounts of time and effort in developing the original concept under the constraints of the IPPNPO will be left with little to show for its pioneering efforts. This conflicts with the foundation upon which the U.S. patent system is built: that risk and innovation are rewarded and future discoveries based on that original risk and innovation adequately compensate the trailblazers (both inventors and investors) for those efforts. This will eventually also affect return on investment for the CIRM itself, as fewer companies choose to participate in technology based on CIRM-funded discoveries because of these onerous provisions and corresponding inadequate risk/benefit ratio.

BIOCOM also notes grave concern on the proposed “March-In” rights. Section II I (4) states that “March-In Rights” may be exercised by CIRM “To alleviate public health and safety needs which are not reasonably satisfied by the grantee organization or its licensee and which needs constitute a public health emergency.” The federal government has the proper authority and expertise to determine a public health emergency and take measures necessary to protect the Union, including licensing alternative manufacturers as necessary in cases of public health emergencies. For CIRM, or any state agency, to assert the right and expertise to suspend patent rights granted by the federal government is a wholly inappropriate exercise of authority by the CIRM.

BIOCOM appreciates and generally compliments the efforts of the staff, advisory committee members, and members of the Independent Citizens Oversight Committee on the comprehensive nature of the IPPNPO. We respectfully implore you, however, to consider the above concerns and possible ramifications if they are not remedied prior to ratification of the final IPPNPO. Thank you for your consideration.

Sincerely,



Jimmy Jackson
Vice President of Public Policy
BIOCOM
jjackson@biocom.org

Ref. 7

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June 16, 2006

BY ELECTRONIC MAIL TO: nonprofitipregs@cirm.ca.gov

C. Scott Tocher, Interim Counsel
California Institute for Regenerative Medicine
210 King Street
San Francisco, CA 94107

RE: Comments on Proposed CIRM Regulation Entitled: Intellectual Property Policy
for Non-Profit Organizations

Dear Mr. Tocher,

The University of California welcomes the opportunity to provide comments on the Intellectual Property Policy for Non-Profit Organizations (IPNPO) adopted by the California Institute for Regenerative Medicine (CIRM) on February 10, 2006.

The University commends the thoughtful and consultative approach that was taken by CIRM in developing this policy. The most important objective of CIRM is clearly the development of therapies to treat and ultimately cure diseases. In meeting this objective, non-profit institutions necessarily rely on industry to invest in the commercial development and production of treatments resulting from academic discoveries. In developing the IPNPO, CIRM had the difficult task of balancing this overarching objective of Proposition 71 with other concerns that were raised after the passage of the Proposition: accessibility and affordability of eventual treatments, the ability to easily march in for a number of reasons, and a desire for the state to share in the rare event that a non-profit research institution receives income from the commercialization of a successful therapy. The issues of access and affordability, in particular, are challenging problems that have been raised on the national level as well, but an intellectual property policy is not the appropriate place to try to address these problems.

Each of the concerns mentioned above is well-motivated, however the cumulative effect may have the unintended consequence of impeding the larger, more important objective of improving public health. The University is concerned that in attempting to address these other concerns, CIRM has erected a

number of barriers that may have a chilling effect on the willingness of industry to invest the necessary resources to ultimately make treatments available to the public.

Furthermore we are concerned that the revenue sharing and other requirements will have the effect of making CIRM funding less attractive to researchers than other funds, and may perhaps even put California at a disadvantage as compared to other states and other countries. While funding for embryonic stem cell research is currently limited, it seems likely that federal restrictions will be lifted in the relatively near future, perhaps not so very long after CIRM grants are eventually made for research. Furthermore, federal funding IS currently available for some of the work that might be done under a CIRM grant, such as research using non-embryonic stem cells or cell lines approved for use with federal funds. And federal funding carries none of the above-mentioned constraints. We also note that other states are following closely on California's heels; while they are making far fewer funds available, they also, at least to date, have imposed far fewer restrictions. All else being equal (or nearly so), industry will be far more likely to invest in an invention that was made without CIRM funds than in one made with CIRM funds.

The following are our specific comments on the Policy, presented in the order in which they appear in the IPPNPO:

100301 (a): As defined, the "authorized organizational official" is the individual "who is authorized to act for the applicant and to assume the obligations imposed by the... conditions that apply to grant applications or grant awards." This is not precisely true at the University, nor, to our knowledge, at most research institutions. The person who signs the grant is usually a contracts and grants officer who has been delegated the authority to execute such agreements on behalf of the institution, but who would never be required to personally assume the obligations of the grant. Those obligations are assumed by the institution, and it would be misleading to represent otherwise. We would recommend the following revisions: "who is authorized to ~~act for~~ execute agreements that legally bind the applicant organization and to assume the obligations imposed by the..."

100301(d): The second sentence of the definition of "biomedical materials" includes a statement that "Specific examples include specialized and/or genetically defined cells,... certain types of animals including transgenic mice and *other intellectual property* such as computer programs." [emphasis added] This implies that biomedical materials are also always intellectual property. However, it is often the case that there is no intellectual property associated with a given biomedical material. To be clear and for CIRM to ensure that the definition includes biomedical materials regardless of whether there is associated IP, the word "intellectual" should be deleted.

100301(g): In the last line, "institutions" should be replaced with "campuses."

100301(h): The definition of grantee organization's share should reflect not only a deduction of the inventor's share, but a deduction for expenses as well, consistent with the concept in 100308. We would recommend the following revision: "...after deducting the direct costs associated with patents and patent applications claiming inventions made under CIRM funding and the inventor's share of those revenues."

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100301(j): It seems that the definition of invention disclosure is intended to capture an enabling disclosure of an invention, whether or not it actually triggers a patent bar. For example, if it were disclosed in confidence, it would still be an invention disclosure, but would not necessarily trigger a patent bar. To be precise, the definition should be modified as follows: "A description of an invention that, if made public, would triggers a patent bar..." Having said that, since it does not appear that this term is used in the remainder of the Policy, it may be more appropriate to simply delete it.

100301(n): To more accurately reflect patent law, the definition of license agreement should be modified as follows: "...to make, use, and/or sell, offer to sell, and/or import."

100301(y): It should be made clear that a research exemption is not intended to permit an entity to use an invention to provide commercial research services to others. This could be clarified with a change such as the following: "...for its own research purposes."

100305(b) and 100305(a): Both of these reporting requirements seem to be already covered in 100302. If that is indeed the intent, it could be made clear by adding the following: "...as described in 100302." If, on the other hand, these are intended to be reporting requirements above and beyond 100302, we would ask that the Policy make it clear how the requirements of 100302 and 100305 differ. More importantly, we note that the reporting requirements under CIRM awards are already rather extensive, and would ask CIRM to consider what it really needs and whether some level of consolidation is possible.

100306(b): The last sentence requires that each license address *all* relevant therapeutic and diagnostic uses of an invention. It is not clear whether "relevant" is meant to include all possible therapeutic and diagnostic uses, or (more appropriately) just those that are included in the license. It is not uncommon for a licensee to pursue only a subset of possible uses under a "field of use" license, leaving other uses available for other licensees. In such cases, it would not make sense for the license to address the uses that are not included in its license. We would recommend that the following be added to the end of the last sentence to make this clear: "...and the licensee agrees to diligently develop."

100306(h): The term "SPO" should be defined either here or in section 100301.

100307: As discussed above for 100301(y), we would recommend that the second line be changed to say: "...for its own research purposes."

100308 – overall: As discussed above, the University is concerned that the revenue sharing requirement will have the effect of making CIRM funding less attractive to research institutions than other funds, and perhaps even put California at a disadvantage as compared to other states and other countries.

100308(a): This provision is written such that the inventor's share seems to be deducted twice, once in the definition of net revenues and again in the requirement of the first sentence, which is clearly not CIRM's intent. We would recommend deleting the following from the second sentence: "inventor's share and."

100308(b): It is our understanding, consistent with the discussion by the ICOC at its meeting on February 10, 2006, is that grantees would share revenues after expenses (i.e., "net revenue") and after deducting the inventor's share. This is not accurately reflected by the language of this section. We would recommend one of two approaches to accurately describe the calculation:

1) Make the change recommended above to the definition of "net revenue" in 100308(a) and in each of the first two sentences of 100308(b) insert the word "net" before revenues; or

2) make the change recommended above to the definition of "Grantee Organization's Share" in 100301(h) and change the first two sentences of 100308(b) to make use of that defined term as follows: "...a threshold amount of Grantee Organization's Share ~~its share~~(after payments to inventors) of any revenues..." and "...25% of Grantee Organization's Share ~~its share~~ after payments to inventors of such revenues..."

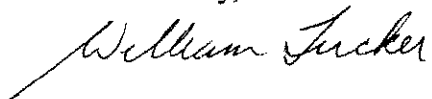
100310(a): As has been raised numerous times, at public meetings and by other respondents, there is a serious concern that the unpredictability introduced by the march-in provision of the IPPNPO may have a chilling effect on industry's willingness to invest the commercial resources necessary to bring a treatment or a cure to market. The march-in provision of Bayh-Dole at the federal level, created such a degree of concern when it was first implemented that many companies were very wary of licensing inventions made with federal funds. It was only after the federal government established a track record of not exercising its right capriciously and the implementation of a fairly rigorous and predictable process that industry began to feel comfortable licensing federally-funded inventions. We believe there is a legitimate concern that CIRM will be much more likely to exercise its march-in right than the federal government has been.

If CIRM feels that it absolutely must include such a requirement, we strongly support the inclusion of a period for cure, as has been done in 100310(b). In addition, we would recommend that the Policy provide for the establishment of a process so that all participants have a better idea of what to expect. In the federal arena, such process is established in the Bayh-Dole implementing regulations at 37 CFR 401.6. To lay the groundwork for this, we would recommend that the first sentence of this section be revised as follows: "With regard to CIRM-funded patented inventions, and generally following the process used by the federal government under the Bayh-Dole Act, CIRM shall..." Finally, we note that the third trigger for march-in, "[t]o meet requirements for public use," is extremely ambiguous. The similar requirement under Bayh-Dole is much more deterministic, since it is "public use specified by Federal regulations." In the CIRM policy it is not clear what would constitute a public use, nor how that determination is made. We would recommend that the this trigger for march-in be deleted from the Policy.

Again, thank you for the opportunity to comment on this important Policy. If you have any questions or would like to discuss any of our comments further, please don't hesitate to contact us. We look forward to seeing the important work of CIRM-funded research begin and are excited about the possibilities for improved public health and the establishment of California as the world leader in stem cell research.

C. S. Tocher
June 16, 2006
Page 5

Sincerely,



William T. Tucker
Interim Executive Director
Research Administration and
Technology Transfer

cc: Deputy Vice Chair Maxon

June 19, 2006

C. Scott Tocher, Interim Counsel
Independent Citizens Oversight Committee
California Institute for Regenerative Medicine
210 King Street
3rd Floor
San Francisco, CA 94107
nonprofitregs@cirm.ca.gov

Re: Proposed Adoption of the CIRM Intellectual Property Policy for Non-Profit Organizations

Dear Mr. Tocher & Members of the ICOC:

The undersigned members of the Research Use Exemption Coalition ("the Coalition") share your commitment to developing and advancing stem cell research and cures. We are dedicated to bringing the promise of Proposition 71 to life, and we applaud your efforts in this regard. We write because of our grave concerns that the Research Use Exemption ("RUE") provision in the proposed regulation, CIRM Intellectual Property Policy for Not for Profit Organizations ("IPNPO"), will stymie the very goals we share in advancing stem cell research and cures and developing innovative therapies for the citizens of California.

As an industry that is largely a home-grown California enterprise, the life science research tools sector is proud that the citizens of our state, including many of our employees, approved Proposition 71 with the very clear intent of supporting the development of new medicines. The intent and wording of the ballot initiative made it clear that the initiative was meant to do one thing: harness the promise that stem cells offer and bring new medicines to Californians. It naturally follows that implementation of Proposition 71 should be based on not only discovering but also developing and disseminating technologies and cures to further this goal. The life science research tools industry is eager to play its role in developing and disseminating research tools as a critical component of the collaborations that will be necessary to realize the goals of Proposition 71.

ADVANCING CALIFORNIA STEM CELL RESEARCH AND CURES

The commercial life science tools industry is a \$17 billion industry largely centered, as noted above, in California. This industry provides essential life science technologies to academic, pharmaceutical, biotechnology and governmental researchers for disease research and drug discovery. Our products can be found in nearly every major laboratory in the world because they provide researchers with, among other things, new experimental capabilities, time and money saving methods and greater consistency.

Coalition members want to support CIRM-funded researchers as they embark on the vital new discoveries that will form the foundation for the next generation of cures and therapies. We are hopeful that CIRM policies will allow us to play an important role in advancing California stem cell research and ensuring California's leading role in the world in developing stem cell cures and therapies. Our companies can transition CIRM-funded discoveries to quality tested, manufactured and distributed products that reach the laboratories of both academia and industry. Unfortunately, the Research Use Exemption provision in the proposed regulation will greatly constrain our ability to participate in CIRM-sponsored collaborations.

THE NEW RUE PROVISION PROPOSED IN THE INTERIM POLICY IS A DRASTIC DEPARTURE FROM CURRENT PATENT LAW

The fundamental policy underlying the patent system is to provide exclusive rights for a limited time to inventors of new and useful technologies in exchange for the full disclosure of those technologies to the public. Such disclosure then promotes further innovation by allowing new technologies to be developed from the foundations established by previous innovators. Furthermore, the exclusivity conferred by patent law promotes innovation by promoting investment in it. The patent system strongly encourages the development of new technologies by balancing the resulting benefits to the public with the interests of inventors.

That being said, the common law doctrine known as the Research Use Exemption to patent infringement allows conduct that would otherwise constitute infringement of the patent when that conduct is purely for philosophical and non-commercial inquiry.¹

As drafted, the CIRM's proposed RUE provision extends far beyond the common law doctrine. The text reads as follows:

e. Requirements to enable research exemption for CIRM-funded patented inventions

1. Grantee organizations agree that California research institutions may use their CIRM-funded patented inventions for research purposes *at no cost*. Grantee organizations shall require the same agreement of each of their licensees of CIRM-funded patented inventions.² (emphasis added)

THE PROPOSED PROVISION WILL STYMIE STEM CELL RESEARCH AND THERAPIES

By broadly requiring that CIRM-funded patented inventions are available "at no cost," the provision proposed in the IPPNPO would block the development and dissemination of any CIRM-supported invention that is used primarily in research. The clause would effectively obligate a grantee or licensee to make his or her invention

¹ *Madey v. Duke University*, 307 F.3d 1351, 1362 (Fed. Cir. 2002)

² IPPNPO, Section H (e);

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available at no cost to what is likely to be nearly the entire American embryonic stem cell research market due to the consolidation of that market in California after Proposition 71. It is unlikely that any company would take on this obligation.

As a result, CIRM-funded research tools will likely either languish on university shelves or be distributed on a limited basis through informal networks of overburdened researchers. It is very unlikely that any for-profit entity would license a research-related invention that cannot be protected in the research environment and that must, in all circumstances, be provided to all California researchers for free. Today, the commercial marketplace serves as a powerful and positive force for licensing and creating important inventions, improving them, producing them and distributing them to all those for whom they have value. If adopted, the current RUE proposal would eliminate these vital marketplace forces.

The consequences for stem cell research and cures in California would be deleterious. As noted above, an “at no cost” regime would preclude any privately funded development and dissemination. This would mean, in turn, that CIRM-funded research and inventions would be *less available* and CIRM inventions would be improved at a *much slower pace* that they would with private support. It seems difficult to deny the likelihood that by effectively eliminating patent protection for research tools, the proposal will cut down on their supply.

Respectfully, there appears to be an implicit misunderstanding in the IPPNPO that research related discoveries emerge “ready to go” from the laboratory and, therefore, that university and non-profit research personnel can effectively disseminate the IP to all of their California colleagues. We strongly disagree. Just as in the case of therapeutics and devices, considerable work is generally needed before research-related IP becomes a broadly available and useful research tool in the hands of end users. Significant effort is often devoted, for example, to combine the IP with other IP or know-how, to establish the parameters of applicability, and to ensure GMP compliance, manufacturability, stability, toxicity and uniformity. Two examples illustrate this point:

- DNA Sequencing: Although the basic Sanger method of DNA sequencing used to sequence the human genome was developed in academia, the sequence of the human genome would not be known today but for commercial high throughput DNA sequencers that were developed by industry. These instruments incorporate IP and other know-how from a variety of technological fields and sources, including for-profit sources, and took significant commercial investment to develop and manufacture. Consequently, these research tool instruments would likely not exist today were it not for effective patent protection, including patent protection extending to research uses.
- Quantum Dot Technology: This revolutionary nanotechnology has the potential to take fluorescent labeling and detection (e.g., tracking stem cells) to the next level. The technology was patented more than a decade ago by

academic institutions, but it did not become a reality for researchers until very recently. Converting this technology into reality required years of private sector investment (exceeding \$40 million dollars) to overcome challenges in manufacturing, stability and derivation.

In a case where (1) an invention is “fully ripe” in the lab and needs no further development, (2) the invention is trivial to duplicate consistently and/or distribute, and (3) the invention has been created in a lab with the resources to promote the invention and field what could be thousands of repeat requests, the proposed IPPNPO scheme could effectively deliver CIRM-funded tools to California researchers. But such cases are, at best, rare. In the more likely case that (a) an invention needs further development, (b) the invention might productively be enhanced through combination with non-CIRM IP or other products, (c) quality manufacture is not trivial, or (d) where inventory and distribution are challenging, the inability for CIRM grantees to obtain effective patent protection for research tool technologies and thereby attract commercial partners will be extremely damaging to the California stem cell research enterprise.

A SOLUTION IN SEARCH OF A PROBLEM

The Research Use Exemption clause in the Interim Policy presumes that there is a genuine functional problem with the current state of the law concerning researchers’ access to IP. Yet this is not the case. As you may know, *the recent National Academy of Sciences-commissioned analysis of the research use matter concluded that patents are not limiting biomedical research, and that licenses when sought for research purposes are generally easy to get and not costly.*³ While we are aware of concerns regarding certain stem cell related intellectual property, we caution the committee not to over-generalize and to change dramatically a system that is overall working very well to the benefit of researchers and patients. Anecdotes should not suffice, given the serious consequences of the dramatic change proposed in the IPPNPO and the enormous risks these changes present.

OTHER PROVISIONS ADDRESS THE GOAL OF BROAD DISSEMINATION OF CIRM-FUNDED RESEARCH

It is our understanding that the committee is interested in promoting the broad dissemination and availability of CIRM-funded IP for California researchers. We support that objective. We believe, as outlined above, that the RUE provision actually works at cross purposes with that goal. In our view, it creates more problems than it solves. Moreover, other provisions in the IPPNPO already address the objective of broad dissemination in a more constructive manner.

Under the IPPNPO (Section H (d)(2)), a grantee may negotiate and award exclusive licenses for CIRM-funded inventions “if such licenses are necessary to provide economic incentives required to enable commercial development and availability.” Section H (d)(3) then requires exclusive licensees to achieve “practical

³ J.P. Walsh, C. Cho, W. Cohen, *Science* **309**, 2003 (2005)

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application” of the IP. Practical application is not defined in the IPPNPO but in federal statute is defined to mean:

The term practical application means to manufacture in the case of a composition of product, to practice in the case of a process or method, or to operate in the case of a machine or system; and, in each case, under such conditions as to establish that the invention is being utilized and that its benefits are, to the extent permitted by law or government regulations, available to the public on reasonable terms.⁴ (emphasis added)

Section H (d)(5) then contains a provision that encourages grantees to apply march-in rights authorities in the event of an exclusive licensee's “failure to keep the licensed invention *reasonably accessible* to the public *for research purposes*.”

Thus, even without the RUE provision in Section H (e), licensees of CIRM funded IP are already required to bring CIRM-funded inventions to practical application and to provide them to “the public” – which surely includes California research institutions – “on reasonable terms.” By adding the RUE provision and its “at no cost” requirement, the Committee, we believe, is working against its own objectives by making it very unlikely that a company will license research-related technology in the first place, even in those cases where commercial licensing is “necessary to provide economic incentives required to enable commercial development and availability.”

THE PROPOSED CLAUSE IS FRAUGHT WITH AMBIGUITIES

There are a number of ambiguities in the proposed language that raise serious questions. These ambiguities include, but are not limited to, the following issues.

First, it is not clear what is intended by the reference to a “California research institution.” How is that term to be defined in the Policy?

Second, the rules that will govern research related IP funded partially by the CIRM are not clear. What does the Committee intend?

Third, given the breadth of the definition of “invention,” to what extent does the requirement “grantee organizations shall require the same agreement of each of their licenses of CIRM-funded patented inventions” extend to technology developed by licensees using CIRM-funded technology?

Fourth, it is not clear what it means that grantee organizations must “agree that California research institutions may use their CIRM-funded patented inventions for research purposes at no cost.” Does this require that grants include a covenant by the grantee not to sue California research institutions for patent infringement based on research uses? Or is more required?

⁴ 37 C.F.R. Section 401.2e (e)

CONCLUSION

Because the RUE clause in the IPPNPO would substantially undermine the incentive to develop and disseminate CIRM-funded research-related discoveries, thus diluting the potential impact of CIRM funding and slowing the pace of stem cell research, we respectfully suggest that it would undermine and constrain the advancement of both research and therapies – contrary to the clearly stated objectives of the CIRM. For the reasons set forth herein, and given that Section H already ensures the broad availability of licensed CIRM IP on reasonable terms, we urge that the CIRM remove the research use clause from the IPPNPO, at least for a period of time during which a full understanding of its implications can be assessed.

Thank you for considering our views. Should you have any comments or questions, please feel free to contact the Coalition through Anthony P. Lakavage, of Applied Biosystems, who can be reached at 650-554-2881.

Sincerely,

The Analytical and Life Science Systems Association (ALSSA)

Applied Biosystems, an Applera Corporation business

BIOCOM

Invitrogen Corporation

Isis Pharmaceuticals

Sangamo BioSciences

Target Discovery



ADVANCING
SCIENCE

Applied Biosystems
an Applera Corporation business

Official Comments to the California Institute for Regenerative Medicine
Notice of Proposed Regulation Adoption:
"Intellectual Property Policy for Not for Profit Organizations."
(regarding the Research Use Exemption provision)

Contact:
Anthony P. Lakavage, JD
Senior Director, Government Affairs and Public Policy
Applied Biosystems
850 Lincoln Centre Drive
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June 19, 2006

Independent Citizens Oversight Committee
California Institute for Regenerative Medicine
210 King Street, Third Floor
San Francisco, CA 94107

Dear Sir/Madam,

I am writing to submit official comments on behalf of the Applied Biosystems Division of Applied Biosystems Corporation to ask that the CIRM Board reconsider the Research Use Exemption ("RUE") provision in the CIRM's "Intellectual Property Policy for Not for Profit Organizations."

Our comments follow. Please feel free to contact me at (650) 570 6667 or Anthony P. Lakavage, JD, Senior Director, Government Affairs and Public Policy at (202) 638 0414 if you have questions.

Regards,

A handwritten signature in black ink that reads 'Dennis A. Gilbert'.

Dennis A. Gilbert, Ph.D.
Chief Scientific Officer
Applied Biosystems

**Applied Biosystems comments to the proposed
CIRM Research Use Exemption provision**

The World's Leading Life Sciences Research Tools Company is a Home Grown California Company that has been developing innovative tools for life sciences researchers for over 25 years.

Applied Biosystems and Celera are businesses of Applera Corporation. Both businesses are based in California and employ over 1800 Californians. Globally, Applera employs 5000. Applied Biosystems is a science and technology company based in Foster City that develops innovative research tools. Celera is based in Alameda and develops novel molecular and other diagnostic tools. Celera, together with Applied Biosystems, were the first companies to map the human genome.

This year is the 25th anniversary of Applied Biosystems. We are looking forward to celebrating our partnership with the science and research community in California and throughout the world in bringing important research tools like gene sequencing technology, mass spectrometry and real time PCR to universities, hospitals, clinics, biotech and pharmaceutical companies and others who develop life saving diagnostics and medicines. It is both the vibrant academic research base of California and the strong intellectual property protection of this country that has enabled us to be successful as a company and to help our customers be successful in bringing diagnostics and therapeutics to patients.

We support the objective of Proposition 71: to bring new stem cell based therapies to Californians to meet unmet medical needs

Like most science and technology-driven businesses, we were gratified by California's leadership in driving the advancement of stem cell research. We believe that stem cells are one of the new frontiers of discovery in biotechnology and are eager to partner with both non-profit and for-profit entities to help unlock the great potential that stem cell research offers. We applaud the efforts of the CIRM to move quickly to help society realize the great potential of this opportunity.

When the voters of California approved Proposition 71, they were very clear in supporting a single goal: to harness the promise that stem cells offer in bringing Californians new therapies for unmet medical needs by directing state supported resources to capitalize stem cell research. This optimism of our citizens is surely based on the immense historic success of the biotechnology industry in developing new therapies. This success has both saved and improved the lives of millions and, at the same time, built a thriving life sciences industry in California.

The commercial life science research tools sector is a \$17 billion industry largely centered, as noted above, in California. The industry provides essential life science technologies to academic, pharmaceutical, biotechnology and government researchers for disease research and drug discovery. Our products can be found in nearly every major laboratory in the world because they provide researchers with, among other things, new experimental capabilities, time and money saving methods and greater consistency.

Applied Biosystems hopes to support CIRM-funded researchers as they embark on the vital new discoveries that will form a foundation for a new generation of cures and

therapies. We are hopeful that CIRM policies will allow us to play an important role in advancing California stem cell research and ensuring California's leading role in the world in developing stem cell cures and therapies.

Life Sciences Research Tools Companies have developed, manufactured, assured quality and distributed some of the most important research tools used for discovery today.

The world-renowned California biotech miracle is predicated on collaboration between academia, industry and government. These collaborations have always been based on good faith and a respect for intellectual property. Moreover, these principles have underpinned the expansion of nearly every area of modern scientific discovery and are the foundation upon which our state's innovation-driven economy is based.

One of the pillars of California's technology industry is the research tools sector. This industry creates the innovations that allow researchers to make discoveries that lead to breakthroughs that save lives with new medications, improve the quality of our environment, support a healthy food supply, detect dangerous pathogens and substances and more. Gene sequencing technology, real time PCR, mass spectrometry and other technologies are required tools for scientific discovery in these areas. Patent protection is essential for their development. Erosion of it will mean fewer discovery tools and fewer innovations.

The proposed research use exemption ("RUE") in the CIRM's IP Policy seems to dismiss the role that research tools companies play in not only discovering and developing new research tools but also in licensing discoveries from academic institutions, validating them, developing quality assurance standards, manufacturing the tools, and distributing them broadly to academia, government, industry and others who pursue bio-medical innovation. It is financially risky to license a discovery and attempt to develop it into an end-user research product. It requires an organized quality and manufacturing capability, a distribution network, sometimes regulatory capabilities and more. Research tools companies perform all these critical roles with the objective of bringing research tools to scientists. We are the partners of researchers, not the adversaries.

If we fail to develop a discovery into a product, research tools companies absorb the cost of the failure. Because of this risk, intellectual property protection is required for us to invest in these endeavors so that when a successful product is developed, we can recover the investment from the failures and attain capital to invest in another project. This model is similar to the later stage model that has led to the development of innovative pharmaceuticals. Without intellectual property protection, pharmaceutical companies could not invest in drug development. Without intellectual property protection, life sciences research tools companies can not invest in new research tools which, in turn would result in fewer new drugs as scientists will have fewer tools to use to make discoveries that lead to therapeutic innovations.

It is easy for Applied Biosystems to provide an important, real-world example of how this successful model of collaboration, based on a foundation of intellectual property protection, has led to the advancement of science. This model of collaboration led to the development of high throughput genomic sequencing which is largely responsible for the development of the genomic revolution that is fueling both scientific discovery and the economy of California today.

The Mapping of the Human Genome

It was 25 years ago that Applied Biosystems was founded, in part, based on a collaboration with the California Institute of Technology (Caltech) which ultimately led to AB developing high throughput genomic sequencing technology.

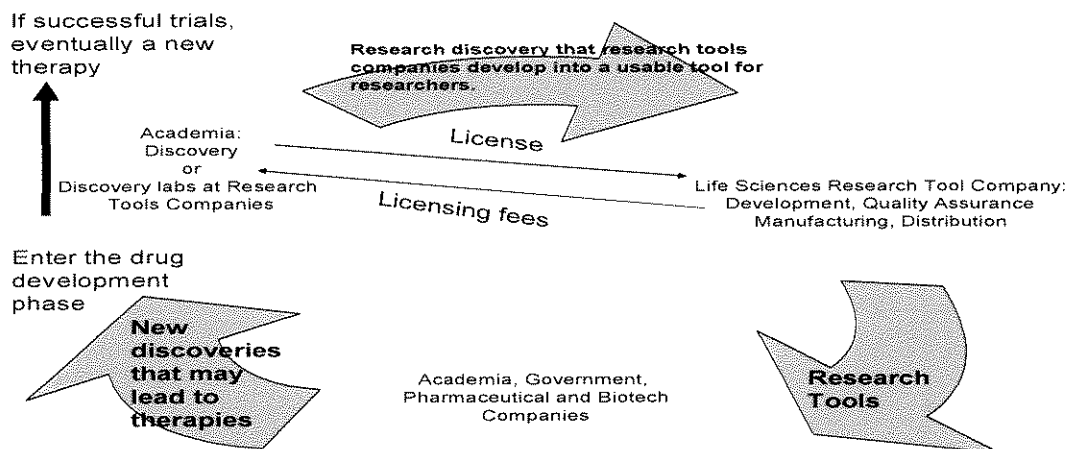
The collaboration between AB and Caltech began with the licensing to AB of the "gas-phase edman degradation" protein sequencer which enabled the detailed analysis of the amino acids of peptides and other discoveries. AB combined these technologies and additional chemical processes with an automatic DNA sequencer. This technology integration led to products such as the four color DNA sequencing instruments known as: ABI370, 373 and 377. The development of these instruments were profound advances for performing DNA sequencing.

Prior to the availability of this technology, DNA sequencing was a labor intensive process that used radioactive labeling of DNA and manual interpretation of the data. Later advances in AB research generated the AB3700 which in turn greatly accelerated the Human Genome Project. Virtually all of the DNA sequencing for the Human Genome project was conducted on Applied Biosystems instruments which would never have been available had it not been for the combination of academic research discoveries at Caltech with the development expertise at Applied Biosystems.

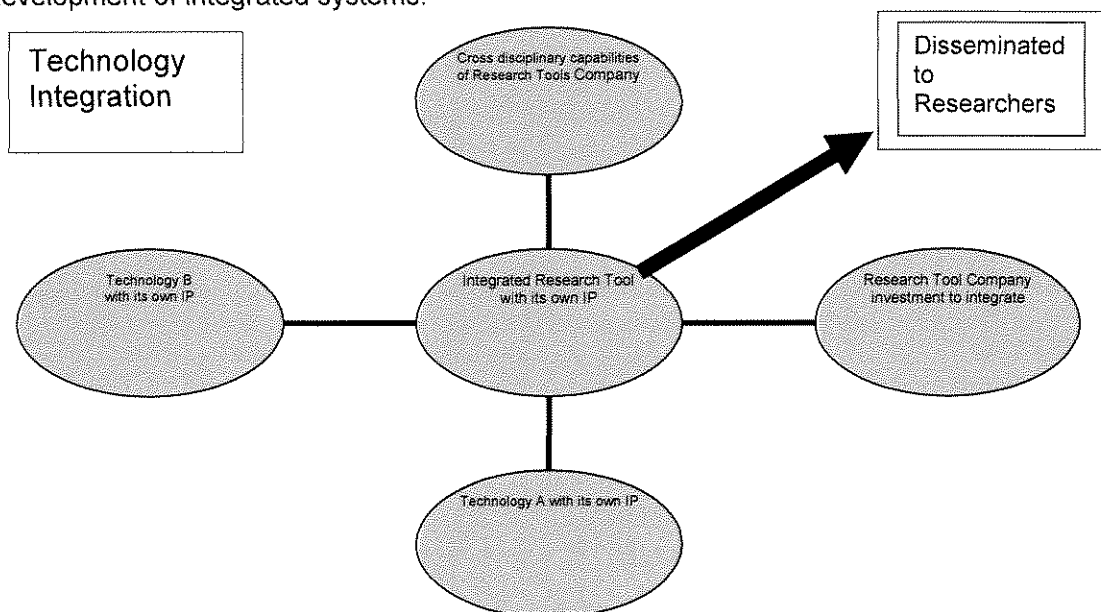
The collaboration between Caltech and Applied Biosystems has made a huge impact on the basic scientific understanding of numerous genomes to date and continues to offer great promise for the future in stem cell research, personalized medicine, pharmacogenomics, forensics and other applications. Moreover, this California collaboration has supported continued investment in research and development at Applied Biosystems and has brought considerable licensing fees to Caltech to support its research programs. It was a collaboration that benefited the collaborating parties, the advancement of science, the economy of California and, most importantly, the patients who are and will benefit from the development of new therapies discovered with this research tool.

DNA sequencing technology is used extensively in drug development today. It will be the underlying architecture upon which the promise of personalized medicine will be realized. High throughput sequencing is only one of dozens of examples of collaborations that have resulted in research tools that have been essential to scientific discovery.

This product development model is dependent upon: 1). early discovery, 2). capital investment (sometimes venture capital), 3). intellectual property protection, 4). manufacturing capacity, quality assurance processes and distribution channels and then, 5). more discovery. The following diagram illustrates the model:



In addition, research tools companies also integrate individual technological developments. Research tools often are comprised of multiple technologies that were developed by various entities. It is the intellectual property associated with those technologies and the IP protection for the technology integrator that enables the development of integrated systems.



Applied Biosystems and other companies could transition CIRM-funded discoveries to quality tested, manufactured and distributed products that reach the laboratories of both academia and industry. Unfortunately, the Research Use Exemption provision in the proposed regulation would likely preclude us from participating in CIRM-sponsored collaborations.

Research shows that patents on research tools do not impede academic research

The Research Use Exemption clause in the Interim Policy seems to presume that there is a real problem with researchers' accessing to research tools with IP. Scientific research indicates the contrary. **The recent National Academy of Sciences-commissioned analysis of the research use matter concluded that patents are not limiting biomedical research, and that licenses when sought for research purposes are generally easy to get and not costly.** (J.P. Walsh, C. Cho, W. Cohen, *Science* 309, 2003 (2005)). The report did not note a single example of a researcher's inability to pursue research because a particular research tool was not made available. Further, federal organizations such as the Secretary's Advisory Committee on Genomics, Health and Society (SACGHS) have considered whether to recommend a federal codification of the RUE and decided to decline making a recommendation to the Secretary of the Department of Health and Human Services for an expansion of the common law RUE. There simply is NO evidence to justify making the drastic change in IP policy that is reflected in the CIRM's proposed RUE.

Prevailing case law already allows researchers to use patented research tools for non-commercial research without infringing on the patent

Prevailing case law currently allows researchers to use patented research tools for non-commercial research without infringing on an existing patent. This exception is the common law Research Use Exemption doctrine, or RUE, to patent infringement. The common law RUE allows conduct that would otherwise constitute infringement of the patent when that conduct is purely for philosophical and non-commercial inquiry.

IP protection encourages investment and disclosure

The patent system is intended to encourage investment in innovative and/or economically risky endeavors by guaranteeing exclusive rights for a limited time to the risk taking investors in exchange for eventual full disclosure of the invention after a pre-determined period. Such disclosure then promotes further innovation by allowing new technologies to be developed from the foundations established by previous innovators. Furthermore, the exclusivity conferred by patent law promotes innovation by promoting investment in it. The patent system strongly encourages the development of new technologies by balancing the resulting benefits to the public with the interests of inventors.

The CIRM RUE Provision discourages investment and disclosure

The CIRM's proposed RUE provision extends far beyond the common law doctrine and would be a massive disincentive for industry to invest in the development of research tools for stem cell research. The text reads as follows:

1. Grantee organizations agree that California research institutions may use their CIRM-funded patented inventions for research purposes **at no cost**. Grantee organizations shall require the same agreement of each of their licensees of CIRM-funded patented inventions. (IPPNPO, Section H (e); emphasis added)

By requiring that inventions arising from CIRM-funded projects must be available "at no cost," the proposed RUE would block the development and dissemination of **any** CIRM-supported invention that is used primarily in research. The clause would effectively obligate a grantee or licensee to make his or her invention available at no cost to what is likely to be nearly the entire American embryonic stem cell research market due to the consolidation of that market in California after Proposition 71. This obligation is not reasonable.

As a result, research tools arising from CIRM-funded initiatives will likely either languish on university shelves or be distributed on a limited basis through informal networks of overburdened researchers. It is unlikely that any for-profit entity would license a research-related invention that cannot be protected in the research environment and that must, in all circumstances, be provided to all California researchers for free. Today, the commercial marketplace serves as a powerful and positive force for licensing and creating important inventions, improving them, producing them and distributing them to all those for whom they have value. If adopted, the current RUE proposal would eliminate these vital marketplace forces. If life science research tools companies do not provide these crucial components of tool development, who will do it?

The consequences for stem cell research and therapies in California would be serious. As noted above, an "at no cost" regime would preclude any development and dissemination. This would mean, in turn, that CIRM-funded research and inventions would be **less available** and CIRM inventions would be improved at a **much slower pace**. It seems difficult to deny the likelihood that by effectively eliminating patent protection for research tools, the proposal will cut down on their supply. The ultimate impact is that the proposed provision would run directly counter to the intent of the voters of California when they voted for Proposition 71 because it will impede rather than accelerate the development of new, stem cell based therapies.

Conclusion: The RUE provision is not in the interest of fostering stem cell research or discovering cures

Research tools companies play a critical role in the development process for new therapies. Our role is to develop discoveries into research tools, manufacture them in a way that assures consistent quality and distribute them to researchers in academia, government and industry. We also aggregate technologies into integrated research tools and invest in their development. These critical functions are only possible with the intellectual property protection that allows for investment. Without these tools, technologies that are critical to the development of new therapies would be unavailable to researchers.

The collaborative dynamic between academia and life science research tools companies has yielded some of the greatest advances in the history of science. A continuation of it should be encouraged in CIRM policy rather than discouraged as it is in the current draft.

While there are multitudes of examples of the impact of innovative research tools on the development of new bio-medical products, there is no evidence whatsoever that patents on research tools impede research. In actuality, there is recent evidence that indicates that patents on research tools rarely have the effect of preventing research.

Voters approved Proposition 71 to accelerate the development of new stem cell based therapies. The RUE provision proposed by the CIRM will inhibit the development of the research tools that will be necessary to harness the promise of stem cell research.

Adoption of the proposed RUE provision would discourage (and potentially stop) all investment in the development of new research tools for stem cell research, slow the progress of stem cell research because researchers would have fewer tools upon which to undertake research and would be counter to the objective of encouraging the development of new cures as expressed by the voters of California when they approved Proposition 71. Accordingly, we urge the Committee not to adopt the proposed RUE provision.

Alternatively, we would urge that the ICOC, at the very least, deliberate further on this matter rather than take action that will signal to California's life science research tools industry that the collaboration that has driven immense innovation in biotechnology in California will not be fostered in CIRM projects.



INVITROGEN CORPORATION

COMMENTS ON
THE CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE
NOTICE OF PROPOSED REGULATION ADOPTION
PROPOSED REGULATION: INTELLECTUAL PROPERTY POLICY FOR NON-PROFIT ORGANIZATIONS

JUNE 19, 2006
NONPROFITPREGS@CIRM.CA.GOV

INVITROGEN
1600 FARADAY
CARLSBAD, CA 92008
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FOR FURTHER INFORMATION CONTACT: JANET LYNCH LAMBERT
DIRECTOR, GOVERNMENT RELATIONS
202 349-4065

June 19, 2006

C. Scott Tocher, Interim Counsel
Independent Citizens Oversight Committee
California Institute for Regenerative Medicine
210 King Street
San Francisco, CA 94107
Transmitted via email: nonprofitipregs@cirm.ca.gov

RE: NOTICE OF PROPOSED REGULATION ADOPTION
PROPOSED REGULATION: INTELLECTUAL PROPERTY POLICY FOR NON-PROFIT ORGANIZATIONS

Dear Mr. Tocher and Members of the ICOC:

At Invitrogen, we want to help bring the promise of Proposition 71 to fruition. We share your goals of advancing stem cell research in order to enable a new generation of therapies and cures. Already we are partnered with many of the world's leading stem cell research laboratories. We provide training and essential tools and technologies that make advanced stem research possible, as well faster, simpler, more efficient, and more consistent. We hope to provide similar support for CIRM-funded researchers, as they embark on the discoveries that will enable the next generation of cures and therapies.

Invitrogen can also play an important role in advancing California stem cell research by transitioning CIRM-funded discoveries from universities and non profits into the marketplace. Regularly, we license technology, invest in it, manufacture it, and distribute it to the research community. As you can see on our website (www.invitrogen.com), more than 20,000 Invitrogen products, many based on technology licensed from academics and non profits, are just a mouse click away for academic, commercial, and government life scientists.

Unfortunately, a brief provision in the Intellectual Property Policy for Non Profit Organizations (IPPNPO), would block the commercialization of any CIRM-supported invention that is used primarily in research. The CIRM-funded research tool IP, therefore, will either languish on university shelves or be distributed at best on a limited (and un-enhanced) basis through informal networks of researchers. Under the existing provision, no private funds will be devoted to improving or distributing CIRM-funded research-related inventions.

The commercial market can be a powerful force that helps advance stem cell research and the development of medical therapies by identifying important inventions, improving upon them, and producing and distributing them to those for whom they have value. We ask that the IPPNPO research use provision be eliminated or modified so that these forces can be used to support the objectives of Proposition 71 in the area of research tools.

What are research tools and why should they matter to the ICOC?

In the life sciences, research tools are typically defined as the full range of products and systems that have their primary usefulness in research or discovery rather than as an FDA-approved product or an integral component of an FDA-approved product. They include but are not limited to bioinformatics, animal disease models, cell lines, cell culture and media, reagents and assays, antibodies, clones and cloning tool methods, cDNAs; expressed sequence tags (ESTs), full-length genes and their expression products; as well as methods and instrumentation for the sequencing of genomes, quantification of nucleic acid molecules, detection of single nucleotide polymorphisms (SNPs), and genetic modifications.

Many research tools are patented. Indeed, the 2005 NIH guidance: *Best Practices for the Licensing of Genomic Inventions*, encourages NIH funding recipients to patent tools “when it is clear that private sector investment will be necessary to develop and make the invention widely available.”¹

Patented research tools have had a profound positive effect on biotechnology and drug discovery, and significant changes in the IP regime underlying research tool innovation and commercialization will affect drug development and patients. Professor Sadao Nagaoka, Director of the Institute of Innovation Research, Hitotsubashi University, recently outlined an analysis of the 47 fundamental patents in life sciences worldwide. Of these “fundamental patents,” he found that 45% were research tool patents, and another 30% were “dual” patents having both end product and research tool applications.²

A May 18, 2006 *GenomeWeb* story appeared under this headline: “*Genomic Tools Helped Drive 52-Percent Jump in R&D Success at Big Pharma; More Business Likely.*” The article summarized the findings of a May 2006 Tufts Center for the Study of Drug Development report:

“Genomic technologies have helped to significantly increase the number of drug candidates that enter clinical trials at the world's biggest pharma,” it said... “TCSDD Director Kenneth Kaitin said discussions he has with officials from big pharma indicate that genomic technologies and methodologies have played “an increasingly important role” in driving the improvement. These tools and methods include mass spectrometry, genome sequencing, gene-expression, high-content screening, and SNP-genotyping. “I don't think there is any question [genomic tools are] playing an increasingly important role in candidate selection for products that enter clinical testing,” Kaitin told GenomeWeb News sister publication BioCommerce Week. “Every company that I speak to now is saying that a significant improvement in their ability to select compounds for clinical development is access to these tools.”

As you appreciate, just as in the case of therapies and devices, research tools don't just happen. Getting robust, high quality, standardized and affordable tools to market takes specialized skills, research, time and investment – even after the initial invention. Considerable testing and surmounting of engineering and scientific challenges is frequently required before widespread distribution and use is feasible. After the product is developed and manufactured, additional

¹ 2005 NIH guidance *Best Practices for the Licensing of Genomic Inventions*. Federal Register: April 11, 2005 (Volume 70, Number 68) Page 18413-18415

² Nagaoka, Sadao, “*An Empirical Analysis of Patenting and Licensing Practices of Research Tools from Three Perspectives*” presentation prepared for the Conference on Research Use of Patented Inventions, organized by the Spanish National Research Council, the Spanish Patent and Trademark Office and the OECD, Madrid 18-19 May 2006. <http://www.oecd.org/dataoecd/20/54/36816178.pdf>

investment is devoted to awareness, dissemination, and technical support for new users. The following three examples reflect common dynamics in the stem cell research domain:

1. Quantum dot technology: This revolutionary nanotechnology has the potential to take fluorescent labeling and detection (e.g. tracking stem cells) to the next level. The technology was patented more than a decade ago by academic institutions, but it did not become a reality for researchers until very recently. To convert this technology into reality required years of investment (exceeding \$40 million dollars) by the private sector to overcome challenges in manufacturing, stability, and derivation.
2. Magnetic beads: This technology provides the power to isolate desired stem and differentiated cells from a mixture gently, efficiently and under GMP conditions. Although the concept may seem simple, a huge R&D investment was required to ensure that the beads were inert, uniform, non-toxic and could be attached to any antibody of choice.
3. Media to grow stem cells: Initial formulations from labs almost always have to be tested on a variety of cells and the formulations tweaked for cost, manufacturability, stability, removal of animal origin components, etc. This takes time, R&D and money. Almost without exception, these investments are made by the private sector.

The IPPNPO research use provision will constrain research and drug discovery

The IPPNPO clearly recognizes the importance of research tools. They are so important, the policy authors appear to have reasoned, that any CIRM-funded invention that has utility in research must be shared with any California researcher at no cost. The research use provision reads:

*"Grantee organizations agree that California research institutions may use their CIRM-funded patented inventions for research purposes at no cost. Grantee organizations shall require the same agreement of each of their licensees of CIRM-funded patented inventions."*³

The problem with this approach, in our view, is that inventions that must be made available at no cost by definition can't be commercialized. No private firm will license a research-related invention that cannot be protected in a research environment and must be made available to all California researchers for free. The clause would effectively obligate a licensee to make the invention available at no cost to what is likely to be nearly the entire American embryonic stem cell research market due to the consolidation of that market in California after Proposition 71. Under those circumstances, we believe no private funding will be used to license the invention and none of the energy of the commercial market will be made available to enhance, manufacture, advertise, disseminate, or support it.

The net effect is that CIRM-funded research-related inventions will be less readily available, and will be improved at a slower pace than inventions created without CIRM support and slower than they would if the CIRM removed the requirement that all its IP be freely available to California researchers. If the media, quantum dot or magnetic bead technologies described above had been developed by a CIRM-funded lab governed by the IPPNPO, the technology would never have reached the market in the form of a useful product. The invention would likely still be sitting in the lab. That is not a good outcome for researchers, and ultimately, a slow-down in research technology development will slow down the pace of drug development itself.

³ CIRM Intellectual Property Policy for Non Profit Organizations, Section II H(e)

As Professor Richard Epstein of the University of Chicago put it in his recent report *Intellectual Property in the Technological Age*:

*"[It is] wrong to think that relaxing patent protection [for research tools] will speed up research for new drug compounds. That argument sees only one side of the problem. Expanding the statutory exemption for downstream users reduces the returns for their upstream suppliers. Effective research depends on the efforts of both. To nullify patent protection for research tools will cut down on their supply. Why take this risk when an ordinary commercial license for research tools could keep matters on an even keel?"*⁴

Two Development Scenarios

- **With IPPNPO Section H (e) research use provision**

- No private investment to further CIRM-funded, research-related inventions
- Universities, Non Profits, and California taxpayers bear full burden of enhancement, production, and distribution of useful inventions
- Commercial researchers are unnecessarily subsidized with free CIRM-funded IP

Dead end CIRM research; Taxpayer, NPO bears full development cost

- **Without IPPNPO Section H (e) research use provision**

- California researcher access to CIRM-funded IP on reasonable terms is assured under Section H(d) and current common law and statutory research use exceptions
- Private investment improves and enhances CIRM funded IP
- Privately held IP and know how is combined with CIRM-funded research-related IP to enable new discoveries
- Private investment assures quality, consistency, and predictable availability of research-related inventions
- Private investment pays for manufacturing facilities and efficient distribution systems (e.g. e-commerce websites) needed to make an invention widely available
- Private investment builds a technical support infrastructure needed to assist researchers using the new invention

**Faster stem cell advances
Industry helps pay for development**

⁴ R. A. Epstein, *Intellectual Property for the Technological Age*, The Manufacturing Institute, April 2006, p. 66

Research use law and policy background

Two justifications for the IPPNPO research use provision are provided in the policy rationale document. The first is that the provision will enhance the development of therapies; our serious concerns with the validity of that argument are outlined above. The second justification is that no general research use exemption currently exists in US patent law, and therefore researchers may be liable for infringement if they engage in unauthorized use of an invention.

There are two research use provisions in current law and practice. One exemption is the judicially created common law research use exemption. This exemption provides that it is not an act of infringement to make and use a patented invention if the use is limited to research or experimentation and the user does not obtain any commercial advantage or benefit.⁵ The second existing research exemption is contained in the Hatch-Waxman Act of 1984.⁶ This "regulatory review" exception removed from patent infringement liability the making and using of some patented inventions for purposes reasonably related to the submission of data to a U.S. government regulatory agency, such as the FDA.⁷ This statutory exemption as well as the common law research use exemption will apply to CIRM grantees absent any additional research use provision in the IPPNPO.

That said, it is the case that patent law affords very few "amnesty" provisions for those engaged in the unauthorized use of another's patent, and that broad exceptions to patent infringement liability have been viewed as damaging to the overall fabric of the patent system, the innovation it rewards, and the disclosure of research advances it insures. Many in the life sciences community have been particularly concerned about an expansion of patent protection exceptions because of the importance strong IP protection plays in sustaining the capital market for biotechnology.

Other kinds of provisions in current law and standard contracts have been used to address the availability of publicly funded intellectual property for the research community without the negative consequences of broad patent protection exceptions. For example, the NIH effectively addresses these issues through various guidance documents, including the Research Tool Guidelines and its Best Practices for the Licensing of Genomic Inventions. These alternative approaches wisely establish a goal of broad IP dissemination, but preserve the possibility of licensing and commercialization where additional private sector investment will support the dissemination goal.

Other provisions in the IPPNPO ensure availability on reasonable terms

The IPPNPO document itself includes important provisions that address IP accessibility, apart from Section H(e).

For example, under the IPPNPO Section H(d)(2), a grantee may negotiate and award exclusive licenses for CIRM funded inventions "if such licenses are necessary to provide economic incentives required to enable commercial development and availability." Section H (d)(3) then requires exclusive licensees to achieve "practical application" of the IP. Practical application is not defined in the IPPNPO but in federal statute is defined to mean:

⁵ *Madey v. Duke University*, 307 F.3d 1351, 1362 (Fed. Cir. 2002)

⁶ 35 U.S.C. §271(e)(1)

⁷ 125 S. Ct. 2372 (2005)

The term practical application means to manufacture in the case of a composition of product, to practice in the case of a process or method, or to operate in the case of a machine or system; and, in each case, under such conditions as to establish that the invention is being utilized and that its benefits are, to the extent permitted by law or government regulations, available to the public on reasonable terms.⁸ (emphasis added)

Section H (d)(3) then contains a provision that encourages grantees to apply march-in rights authorities in the event of an exclusive licensee's "failure to keep the licensed invention reasonably accessible to the public for research purposes."

Thus, even without the RUE provision in Section H (e), exclusive licensees of CIRM funded IP are already required to bring CIRM-funded inventions to practical application and to provide them to "the public" – which surely includes California research institutions – "on reasonable terms." By adding the RUE provision and its "at no cost" requirement, the Committee is undermining its own goals by making it very unlikely that a company will license research-related technology in the first place, even in those cases where commercial licensing is "necessary to provide economic incentives required to enable commercial development and availability."

Research Use of IP without IPPNPO Section H (e)

Non-commercial philosophical inquiry infringement	Covered by common law research use exception
Commercial research use infringement	Drug and device research related to FDA submissions is covered by the Hatch-Waxman exception
Exclusive licensees of CIRM-funded IP	Under section H (d)(2)(3)(5) terms, licensees must "achieve practical application" (make available to the public on reasonable terms) and may risk march-in if they fail to keep the invention "reasonably accessible to the public for research purposes"
Authorized Research Use	Academic and non profit researchers who sought authorization to use another's IP for research purposes found it inexpensive to obtain, and delays were rare ⁹

What problem is being solved?

Given that (1) a good deal of drug development and device-related research is covered by an infringement exception, (2) philosophical non-commercial research is already covered by an existing research use exemption, (3) other provisions in law and the IPPNPO allow research funders to ensure the availability of key IP for research, and (4) licenses are generally very readily available to researchers who seek "authorized use" of inventions¹⁰, why is an additional, broad research use provision – one with so many negative unintended consequences – required in the IPPNPO?

⁸ 37 CFR Sec 401.2(e)

⁹ J.P. Walsh, C. Cho, W. Cohen, *Science* **309**, 2003 (2005)

¹⁰ Ibid

Members of the CIRM community sometimes point to a specific case in which an important research tool has not been made as readily available as the research community would like. It is not our contention that the current system is perfect, but rather that it works well almost all the time. To address the occasional problem, we should not undermine a productive and effective patent system that has enabled the fastest and most widespread advances in medical research and healthcare treatment in human history. This is especially true given that alternative remedies to the few problem cases already exist. In our view, the IPPNPO proposal undermines a 99% effective system in order to solve the 1% problem.

Academic researchers conclude research access to IP is not an issue

One need not rely on our assessment of the effectiveness of the current system. Recent academic studies have examined exactly the question at issue here: Are biomedical researchers hampered by patents and IP licensing requirements? The answer, according to the recent studies, is no.

- In 2003, a small sample interview study suggested that, despite numerous patents on upstream discoveries, academic researchers have accessed knowledge without the anticipated frictions.¹¹
- In September 2005, Walsh, Cho, and Cohen published findings from a National Academy of Sciences-commissioned survey of 414 biomedical researchers in universities, government, and nonprofit institutions. They concluded, "Our results offer little empirical basis for claims that restricted access to IP is currently impeding biomedical research."¹² Among their findings:
 - "Although common, patents in this field are not typically used to restrict access to the knowledge that biomedical scientists require"
 - "No one reported abandoning a line of research"...none were stopped by the existence of third party patents, and even modifications or delays were rare affecting around 1% of our sample."
 - "In addition, 22 of the 23 respondents...reported that there was no fee for the patented technology, and the 23rd respondent said the fee was in the range of \$1 to \$100."
 - "Thus, for the time being, access to patents on knowledge inputs rarely imposes a significant burden on academic biomedical research."¹³
- In May, 2006, the American Association for the Advancement of Science (AAAS) reported the results of its survey of more than 8000 of its US members (2157 respondents across industry, government, academia and non profits).
 - Even when including industry respondents, AAAS found that obtaining IP caused a research delay for fewer than 5% of life sciences/medical & health/biological sciences respondents. In addition, fewer than 4% of those respondents were prompted to change the direction of their research due to IP accessibility, and only about 1% abandoned their research due to difficulty obtaining IP.¹⁴ It was also

¹¹ J.P. Walsh, W.M. Cohen, A. Arora, *Science* **299**, 1021 (2003)

¹² J.P. Walsh, C. Cho, W. Cohen, *Science* **309**, 2003 (2005)

¹³ Ibid

¹⁴ J. Asher, *Access to Patented Technologies: Results of a Survey of the AAAS Scientific Community*, presentation given at the Conference on Research Use of Patented Inventions, organized by the Spanish National Research Council, the Spanish Patent and Trademark Office and the OECD, Madrid 18-19 May 2006.
<http://www.oecd.org/dataoecd/20/52/36816036.pdf>

noted during the OECD meeting discussion of the AAAS findings that a goal of the patent system is to avoid duplication in research, so that a change in research direction due to IP consideration is not necessarily a negative outcome.

These studies indicate that despite worries in the wake of the 2002 *Madey* decision, access to IP is not currently a routine problem for researchers. In light of this data, we ask the ICOC not to implement a dramatic new research use provision in an effort to solve an anticipated problem.

Our Request

Because we are convinced it will limit the advancement of stem cell research and the development of new treatments, we request that you remove the current research use provision in Section H (e). We believe that current research use law and practice, combined with the requirements contained in Section H (d) will achieve your goal of broad and rapid dissemination of important CIRM-funded research-related inventions to California researchers far better than would the research exception provision in the IPPNPO. Moreover, we believe such an approach would avoid many of the unintended negative consequences of Section H (e), and allow the CIRM to harness private investment in support of your goals.

Should you conclude, nevertheless, that some provision is absolutely necessary, we ask that it adhere to three principles:

1. Do no harm to the academia-industry research tools partnership that is currently working well nearly all the time – to the benefit of researchers and patients
2. Focus on the *goal* of providing broad access for California researchers to CIRM funded IP, not the *means*
3. Preserve the opportunity for the private sector to invest its own time, money, and effort in support of your mission and your goals – in the research tools domain as well as in therapeutics and devices.

On behalf of Mahendra Rao, Ph.D., Vice President of Stem Cell R&D, and Invitrogen's 1500 California –based employees, I thank you for your attention to our concerns. Please feel free to contact me if we can be of any further assistance.

Sincerely,



Greg Lucier
Chairman & CEO

GTL / sdr

Ref. 11

Scott Tocher

From: Jesse Reynolds [jreynolds@genetics-and-society.org]
Sent: Monday, June 19, 2006 3:19 PM
To: CIRM Nonprofit IP Regs Comments
Subject: comment on Intellectual Property Policy For Non-Profit Organizations

Dear CIRM,

On behalf of the Center for Genetics and Society, I submit the following single comment on the Intellectual Property Policy For Non-Profit Organizations.

The final section, 100310, on March-In Rights, should explicitly state that the Attorney General has the authority to enforce the march-in rights on behalf of the state. There has been some ambiguity on this matter, although at the February 10, 2006 ICOC meeting CIRM counsel James Harrison asserted that the Attorney General does have this right. However, stating this in the regulations will clarify the matter.

Thanks,
- Jesse Reynolds

Jesse Reynolds
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7/7/2006

Comments on CIRM Non Profit Organizations IP Regulations

Submitted by Ken Taymor / ken@mbvlaw.com

§ 100300. Intellectual Property Requirements for Non-Profit Organizations - Scope.

This section should be modified to make clear the intent of CIRM in "appl[ying]" new regulations to "currently active grants[.]" In particular, the regulation should make clear (if this is CIRM's intention) that (1) new regulations will be effective as of the later of the effective date of the regulation or "the start date of the next non-competitive renewal period[;]" and (2) by "applied to" CIRM means that the requirements of the new regulation apply to actions taken and agreements entered into after the effective date of the regulation, and do not require any modification of licenses or other contracts relating to the research funded by the grant which have been executed prior to the effective date of the regulation.

The term "currently active grants" should be clarified.. For example, what regulations (new or original at the time the grant was funded) will apply to a license that a grantee institution negotiates with respect to an invention made under a CIRM grant after the grant has been completely funded, all grant funds have been expended by the grantee, and all post-grant reporting has been completed?

The second to last sentence should be modified to provide that a failure by a PI or other person affiliated with the grantee to have notification shall not excuse non-compliance as long as CIRM has notified the grantee.

§ 100301. Intellectual Property Regulations - Definitions.

The definition "(g) 'Grantee/Grantee Organization.'" creates confusion in the regulations. The words "individual or" should be deleted if the regulations are, as stated, only for grants to Non-Profit Organizations, which by definition may not be an individual. The term "organization in the first line should be changed to the defined term "Non-Profit Organization" since these regulations are supposed to apply only to non-profit organizations and without this change there is no clear limitation on their scope to these kinds of entities. In addition, the term is not used consistently. References to "Grantee institution[.]" a term that is not defined, should be changed to Grantee Organization, and all references to Grantee Organization should use initial caps (there are many references to "Grantee organizations" in the regulations). Finally, it is preferable in regulatory drafting to use a single defined term for a single meaning. As there does not seem to be any need for alternating between the terms Grantee and Grantee Organization, just the latter term should be used.

The following changes are suggested:

(s) "Non-Profit Organization." A (1) university or other institution of higher education or an other organization that is of the type described in 501(c)(3) of the Internal Revenue Code of 1954-1986, as amended (26 U.S.C. 501 (c)(3)) and is exempt from taxation under 501 (a) of the Internal Revenue Code (26~~5~~ U.S.C. 501 (a)) or (2) any other non-profit scientific or educational organization qualified under a state non-profit organization statute whose organizational charter provides that (a) the organization is not organized or

operated for the private gain of any Person, (b) no part of the organization's net income or assets shall inure to the benefit of any Person, and (c) the organization's net assets, upon dissolution, are shall be distributed to a nonprofit fund, foundation or corporation which is organized and operated exclusively for charitable purposes.

Reasons: For profit universities and institutions of higher learning should be excluded from the scope of these regulations. The 1954 IRC is no longer in effect. The additions at the end of the definition exclude from the applicability of the regulations a mutual benefit non-profit corporation whose members are for-profit entities.

In addition, CIRM should consider whether it is appropriate to consider within the scope of these regulations, grantee organizations that are governmental entities, such as hospitals or departments of public health. If so, the definition should be changed accordingly.

The following terms do not appear to be used in the Regulations and should be deleted.

(f) "For-Profit Organization."

(u) "Office of Technology Transfer."

(y) "Research Exemption." (used only in Section Heading, but the terms of the exemption are set forth in the body of the regulation. The defined term confuses the statement of the exemption set forth in the body of the regulation because it is not clear whether the definition is intended to modify the text of the regulation. The definition suggest that the research exemption should be measured in terms of the absence of a state of fear in the mind of a researcher and that the research exemption does not prevent a patent holder from seeking an injunction against research using the patent (as long as no payments are demanded).

(z) "Research Tool."

Definitions of the following terms should be provided:

"Exclusive license"

"Non-exclusive license"

"California research institution"

"Research purposes"

"Person"

Reasons: The terms exclusive and non-exclusive license are used throughout the regulations and impose substantially different rights and obligations on grantees and licensees depending upon which category the license falls into. A particular concern is that materials circulated CIRM in connection with the regulations suggested that the term non-exclusive license included all licenses for an invention if the licenses divided the market into exclusive parts. This would mean, for example, that if a grantee licensed an invention to a commercial entity for all therapeutic purposes within the United States, Asia, Africa and the European Union, the license would be considered "non-exclusive" as long as the grantee also licensed the invention for the same purposes in a non-EU European nation. Similarly, if a license is exclusive for the field of cardiomyocytes, but not for all other fields, these CIRM materials suggested it is a non-exclusive license. It seems in both cases, however, the special requirements imposed by the regulations on

exclusive licenses (such as having plans for providing access to therapies by uninsured Californians), should apply to such licenses. Moreover, if these licenses are considered non-exclusive under the regulations, they undermine the arguments presented to the public that the regulations broadly encourage competitive, non-exclusive licensing and they would not be subject to march in rights or required development milestones, thereby allowing license banking and use of licenses to block development of competitive therapies and diagnostics.

A definition of “Research Purposes” is important to clarify, inter alia, the meaning of the Research Exemption provided under the regulations. For example, the definition should be used to make clear that the CIRM research exemption is intended to be and is broader than the federal research exemption because the term research purposes, and to make clear whether the term as used in these regulations should be interpreted similarly or differently from the definition of the “research” as used in connection with human subjects protection under federal law and in connection with the CIRM Medical and Ethical Standards. A suggested starting point is the definition of research as “a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge. Activities which meet this definition constitute research for purposes of these regulations, whether or not they are conducted or supported under a program which is considered research for other purposes. For example, some demonstration and service programs may include research activities.” [45 CFR 46.102(d)].

The definition of California research institution should include a clarification of whether the institution must be exclusively, primarily, or minimally involved in research, and what level of presence in California is necessary for the research institution to be a California research institution. For example, if only a minimal contact is required, any entity could rent a mail drop in California while conducting all of the exempt research out of state (or out of country).

The bracketed language in the definition of “Invention” should be deleted.

§ 100304. Biomedical Materials.

See comments on need for definition of “research purposes.”

Replace “at cost” at end of last sentence of regulation with “at the actual cost of providing the material without an allocation of costs for overhead, research, discovery or other non-direct costs of providing the material.”

§ 100305. Patent Applications.

Add at the end of (a) “This requirement shall not restrict the rights of Grantee Organizations to recover these costs through license fees or otherwise.”

§ 100306. Licensing CIRM-Funded Patented Inventions.

See comments on definitions of exclusive and non-exclusive licenses and need for definition of “Person.”

(d), line 21; Replace “only to organizations” with “only to Persons”

Reason: A licensee may be an individual, a group of individuals or entities other than an “organization”. A conventional legal definition of Person will help keep clear that the grantee / licensor subject to these regulations is a Non-Profit Organization, but the licensee may be any individual or entity.

(e), (f) and (h) should be combined into a single monitoring and enforcement section. A particular concern is that as divided and drafted, (h) imposes a mandatory but ambiguous obligation on grantees (“Grantee organizations shall [emphasis added] take administrative action . . . where necessary”) [who determines when action is necessary and what standard is to be applied by the decisionmaker] while (e) and (f) more appropriately delegate discretion in enforcement to the grantee.

§ 100307. Research Exemption.

See comments in definition section on Research Exemption, research purposes and California research institution.

§ 100308. Revenue Sharing.

(c) The regulation should clarify how to calculate the State of California’s share when multiple sources supported the creation of CIRM-funded patented inventions. Several concerns can be addressed by clarifying the cost sharing formula. The objective should be to minimize record keeping burdens of allocating overhead, general support and other contributions, while providing the state with a fair return. In addition, if another funding source does not require any revenue sharing, should that funding source’s contribution be used to reduce the share of revenues payable to the State?

§ 100310. March-In Rights.

See comments on definition of exclusive and non-exclusive licenses.



center for advanced
study & research on intellectual property

CASRIP

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June 19, 2006

SENT VIA EMAIL: nonprofitpregs@cirm.ca.gov

C. Scott Tocher
Interim Counsel
California Institute for Regenerative Medicine
210 King Street
San Francisco, CA 94107

Re: IPPNPO

Dear Mr. Tocher:

Having followed and commented¹ with great interest on the developments of Proposition 71, the ICOC, and CIRM, I am submitting the follow constructive comments on the proposed IPPNPO. These comments are my own and do not necessarily reflect the views of either CASRIP or the University of Washington. While I am uncertain whether it is appropriate for an individual residing outside of the State of California to make comments during this public comment period for California state regulations, the potentially wide impact of these regulations may well reverberate outside of California's borders. If, however, you deem it improper for an outsider to submit such comments, then please disregard this letter and take no offense from the submission.

The substance of my comments falls into three separate categories. First, there may be possible unintended consequences emanating from CIRM's establishment of a

¹ See Sean M. O'Connor, *The Use of MTAs to Control Commercialization of Stem Cell Diagnostics and Therapeutics*, BERKELEY TECH. L. J. (forthcoming 2006 Symposium Issue); Sean M. O'Connor, *Intellectual Property Rights and Stem Cell Research: Who Owns the Medical Breakthroughs?*, 39 NEW ENG. L. REV. 665, 675-679 (2005); Sean M. O'Connor, *Public-Private Partnerships and De Facto Research Use Exemptions: Case Study of the Thomson Stem Cell Patents*, MAINE L. REV. (forthcoming 2007); Sean M. O'Connor, *Public-Private Partnerships and De Facto Research Use Exemptions: Case Study of the Thomson Stem Cell Patents* (presentation at CSIC/OECD/OEPM Conference, "Research Use of Patented Inventions" Madrid, Spain, 18-19 May 2006) available at <http://www.oecd.org/dataoecd/40/25/36817472.pdf>.

shadow or mirror Bayh-Dole system versus a system that is truly consistent with Bayh-Dole. Second, there may be significant impediments to the continued growth of a robust research tools industry in California based on the numerous requirements for access of CIRM funded technology and materials at or below cost to the provider. And third, the potential financial disincentive of strong recoupment provisions for CIRM funded intellectual property.

I. Shadow Bayh-Dole System vs. System Consistent with Bayh-Dole

In my 2005 article in the *New England Law Review*,² I argued that CIRM should adopt an IP allocation system that would be consistent with the system of allocating IP rights for federally funded inventions established by the Bayh-Dole Act of 1980 (“Bayh-Dole”).³ Numerous other commentators appear to have suggested the same thing. And, in fact, the IPPNPO are clearly modeled on Bayh-Dole. However, there is a difference between creating an IP allocation system that shadows or mirrors the federal Bayh-Dole system and one that is instead simply consistent with Bayh-Dole. To wit, by including its own version of march-in rights in the IPPNPO, CIRM begs the question of what would happen if – likely when now – federal funding has also been used for a CIRM funded invention and both the federal funding agency and CIRM elect to exercise their respective march-in rights. It may be that both governmental entities would choose the same third party to license the invention to for more diligent commercialization, but this may also not be the case. One would assume that the federal agency choice would trump under some use of the supremacy doctrine for conflicts between federal and state law. But CIRM nonetheless is establishing a potential conflict – and likely one in which it will always be the loser. Accordingly, CIRM may want to review the IPPNPO again with an eye to whether it is simply creating a “mini-me” state version of Bayh-Dole, or a system that is truly consistent with the federal Bayh-Dole system (and hence might look different in some material provisions).

II. At or Below Cost Access as an Impediment to California Research Tools Industry

In Sections H(b)(1) and H(e), CIRM will require that CIRM funded inventions and materials must be provided by their owners for free, or at or below cost, to other California research institutions. Notwithstanding the vagueness – and potential broad interpretation – of the term “California research institution,” these financial limitations may significantly harm the California research tools industry. They may also negatively impact research institutions themselves who create such tools or materials, as those entities may find themselves as victims of their own success when large numbers of requests for access begin pouring in.

For Section H(e) in particular, I humbly suggest the following substitute language:

² Sean M. O’Connor, *Intellectual Property Rights and Stem Cell Research: Who Owns the Medical Breakthroughs?*, 39 NEW ENG. L. REV. 665, 675-679 (2005).

³ P.L. 96-517, 94 Stat 3015 (1980) (codified at 35 U.S.C. § 200 *et seq.*).

Grantee organizations agree to provide unbiased access to CIRM-funded patented inventions to California research institutions for use in their internal non-commercial research at reasonable cost. If a grantee's CIRM-funded patented invention is made broadly commercially available at reasonable cost to California research institutions, then the grantee's obligation shall cease.

III. Overly Strong Recoupment Provisions

I was delighted to see a recoupment provision in the IPPNPO, as I have long believed that the proposed recoupment provision of an earlier version of Bayh-Dole should have remained in place. However, my vision of a recoupment provision has always been one that stays true to the sense of the term that seeks only repayment of money lent or granted. In other words, recoupment should work more like debt and not equity. CIRM's recoupment provision instead gives the unlimited upside characteristic of equity. This might mesh well with a view of CIRM as a virtual part owner of the invention based on its original investment. But, it could also significantly chill downstream venture and other risk capital investment who will not want to essentially take on CIRM as another equity partner in their investment. Accordingly, CIRM should cap the recoupment on successful CIRM funded inventions once CIRM has recouped all of its original funding, perhaps plus some small extra return in the nature of interest or similar cost of lending fee.

Conclusion

The IPPNPO are a great start to IP allocation by CIRM. I understand that there are many constituencies that CIRM has to satisfy in its work. It is my hope that these comments help CIRM continue to strike a reasonable balance among the interests of all of its constituents.

Best Regards,

A handwritten signature in black ink, appearing to read 'S. O'Connor', with a long horizontal flourish extending to the right.

Sean M. O'Connor, J.D., M.A.

Pamela Samuelson, Prof. of Law, Director
Robert Barr, Executive Director
Alissa Centivany, Research Fellow

Berkeley Center for Law & Technology
University of California, Berkeley
School of Law, Boalt Hall
355 Boalt Hall
Berkeley, CA 94720-7200

Dated: June 19, 2006

SENT VIA EMAIL: nonprofitipregs@cirm.ca.gov

C. Scott Tocher
Interim Counsel
California Institute for Regenerative Medicine
210 King Street
San Francisco, CA 94107

Re: Intellectual Property Policy for Non-Profit Organizations

Dear Mr. Tocher,

The Berkeley Center for Law & Technology ("BCLT") has its mission: to foster beneficial and ethical advancement of technology by promoting the understanding and guiding the development of intellectual property and related fields of law and policy as they intersect with business, science and technology. Consistent with this mission, we offer below some comments and recommendations on the draft Intellectual Property Policy for Non-Profit Organizations ("draft IP policy") promulgated by the California Institute for Regenerative Medicine ("CIRM").

Our interest in offering these comments and recommendations is an outgrowth of the experience one of us, Pamela Samuelson, had in serving on the Intellectual Property (IP) Study Committee convened by the California Council on Science and Technology

(CCST) to study and make recommendations about the IP policy that should be adopted for state-funded research such as that authorized by Proposition 71 that authorized the creation of CIRM. Samuelson, now a member of CCST, has also served on two IP study committees convened by the National Academies of Sciences. She has been teaching and writing about IP law for more than twenty years and is the Richard M. Sherman distinguished Professor of Law at UC Berkeley and a Director of the BCLT.

Before coming to Boalt to serve as the Executive Director of the BCLT, Robert Barr practiced IP law for over 20 years, most recently as vice president for intellectual property and worldwide patent counsel for Cisco Systems where he was responsible for all patent prosecution, licensing, and litigation. He was an adjunct professor of patent law at Hastings College of Law. In addition, Mr. Barr is a frequent speaker on patent reform issues and has testified before the Federal Trade Commission regarding intellectual property law and policy.

Alissa Centivany is the Microsoft Research Fellow at the BCLT. Prior to her fellowship, she graduated with high distinction from the University of Michigan, Ann Arbor, and was awarded her JD, with distinction, from Wayne State University Law School.

We believe we are in a good position to assess and offer suggestions to CIRM on the draft IP policy. We and our colleagues at BCLT are a source of unparalleled expertise on intellectual property law as witnessed by the fact that, for nine years in a row, BCLT has been ranked as the best IP program in the nation.¹ Through her service on the CCST IP study committee, Samuelson realized that there was a need for ongoing work to be done in this area to address some important details that the CCST report did not address. As a first step, BCLT and the Berkeley Technology Law Journal (BTLJ) organized a conference, bringing together some of Berkeley's most accomplished innovation scholars and outstanding scholars from other universities to provide reflective suggestions on

¹ U.S. News & World Report, http://www.usnews.com/usnews/edu/grad/rankings/law/brief/lawsp05_brief.php (last visited June 19, 2006).

CIRM IP policies and other legal and policy challenges of the California Stem Cell Initiative.²

The Stem Cell conference, which was held on March 2-4, 2006, brought together a diverse group from all over the country, representing a wide range of perspectives. Members of UC Berkeley faculty and other non-profit research institutions, the biotechnology industry, patient advocacy groups, the general public, and policy-makers converged at Boalt Hall to discuss and debate aspects of this important initiative and the challenges of implementing Proposal 71. Some of the key points of concern for conference participants are woven into the comments that follow. (The program for this conference is attached as Appendix A.)

We do not purport to speak for all BCLT Directors, but hope that our reflections on the draft CIRM IP policy will be helpful. Our recommendations are aimed at furthering CIRM's goals of promoting academic openness and rapid translation of research results into products through effective commercialization. Also attached as appendices are drafts of three papers presented at the Stem Cell conference that address IP issues; final versions will be published in the forthcoming Berkeley Technology Law Journal's Symposium Issue.

1. We support CIRM's draft policy insofar as it follows the Bayh-Dole model.

The dual goals asserted by CIRM in its draft IP policy, academic openness and ensuring that scientific advances are widely available to the public via commercialization, are furthered by allowing universities to patent discoveries produced as a consequence of CIRM grants. Transforming promising research results to marketable products will require venture capital and other capital investments for which exclusive rights are necessary.

² The Stem Cell Symposium was co-hosted by the Berkeley Center for Law and Technology, the Berkeley Technology Law Journal, the Berkeley Center for Law, Business, and the Economy, and the Berkeley Traver's Program on Ethics and Government Accountability. Information on the conference, including schedule, list of participants, and conference audio can be found on BCLT's website: <<http://www.law.berkeley.edu/bclt>>

Furthermore, in the future, perhaps near future, there may well be federal funding for human embryonic stem cell research as to which Bayh-Dole will apply. CIRM's draft policy is forward-looking in its consistency with that Act.

2. We applaud CIRM as to its refinements of Bayh-Dole.

CIRM has improved upon the Bayh-Dole model by clarifying timing requirements. Bayh-Dole relies on fairly vague terms to effectuate its policy of open sharing. For example, § 202(c)(1) of that Act requires that the grantee organization disclose inventions to a funding agency within a "reasonable time." By contrast, CIRM creates a clearly defined 60-day window during which funding recipients must perform a variety of reporting requirements: §100302(a) grantees have 60 days to notify CIRM of disclosed funded inventions; §100303(b) grantees have 60 days to submit an abstract and biological description, fit for public consumption, of published research findings; §100304(c) grantees must share biomedical materials described in publication within 60 days of request.

CIRM has further improved upon the federal model by explicitly providing for a research exemption. While Bayh-Dole is silent on the issue, in *Madey v. Duke*, 307 F.3d 1351 (2002), the Federal Circuit explicitly stated that the "experimental use" exemption did not extend to the activities of research institutions. By contrast, CIRM provides for just such a right in §100307 which grants California research institutions permission to use CIRM-funded patented inventions for research purposes at no cost.

Finally, CIRM has improved upon the Bayh-Dole model with regard to "march-in" rights. Bayh-Dole's "march-in" provisions are prohibitively cumbersome to administer; §202(a)(ii) of that Act states that an agency may restrict or eliminate a grantee's patent rights only in "exceptional circumstances," §203(a) states that an agency may "march-in" only if it determines the action is necessary and §203(b) states that such determination will be held in abeyance pending the exhaustion of all appeals. The combined

application of those provisions is so cumbersome that enforcement has been deterred; no federal agency has ever exercised its “march-in” rights. By contrast, in §100310(b), CIRM replaces Bayh-Dole’s administrative obstacles with a clear indication that march-in rights will not be exercised until the grantee (or licensee) has been given notice and up to a one-year window to cure the deficiency.

3. We suggest that CIRM consider making three further refinements of its policy.

First, grantees should be given discretion to decide not to patent certain discoveries that might otherwise qualify for patent protection where exclusionary rights are not needed to promote CIRM’s goals.

Bayh-Dole presumes that patents are always needed to promote utilization of inventions arising from government funding, but this is not so:

“Whatever the merits of this presumption for patents on downstream inventions such as new drugs, it makes little sense for patents on broadly enabling upstream research technologies that are ready for dissemination to researchers in both the public and private sectors and may be put to use in the laboratory without further investment in developing them as products.”³

We believe that CIRM should provide discretion to grantees to decide not to patent where acquisition of exclusive rights would slowdown or impede progress, rather than promote it.

Second, for broadly enabling research tools and other upstream innovations referenced above, CIRM should create an explicit presumption in favor of non-exclusive licenses. In §100306(b) CIRM states that grantee organizations shall negotiate non-exclusive licenses of CIRM-funded inventions “whenever possible.” This is a step in the right direction, but we think it would be better to create an explicit presumption in favor of

³ Arti K. Rai and Rebecca S. Eisenberg, *Bayh-Dole Reform and the Progress of Biomedicine*, Law and Contemporary Problems, Vol. 66, No. 1, at 17. This paper may be downloaded without charge from the Social Science Research Network Electronic Paper Collection: http://www.ssrn.com/abstract_id=348343 (last visited June 19, 2006).

non-exclusive licenses and require grantees to justify deviations from this presumption. This is particularly important with respect to broadly enabling research tools.

The provisions guiding grants of exclusive licenses, §100306(b), (c), (d), & (e), should remain intact "as is." We agree that, in some circumstances, exclusive licenses will be necessary to provide economic incentives required to enable commercial development and availability of the inventions, for example with downstream diagnostic and therapeutic tools. When paired with an explicit presumption of non-exclusivity, the remaining provisions in this section provide a good mechanism for limiting the grant of exclusive licenses to occasions when they are truly necessary.

Finally, in his presentation at the stem cell conference, Boalt Hall Professor and BCLT Director, Robert Merges, agrees with CIRM's policy insofar as it supports rapid and effective commercialization of basic and applied research results. He also agrees with the means used to accomplish this: giving commercial licensees – pharmaceutical and biotechnology firms, typically -- wide latitude to develop commercial products based on the research. Professor Merges suggests, however, and we agree, that in order to protect against egregiously unfair practices by commercial developers down the line, CIRM should retain the right to revoke a license under specific (and likely very rare) circumstances, including persistent, excessively high pricing of commercial products based on CIRM research. Such a provision, he adds, should take into account not only the actual price levels, but also any program in place to lower the effective cost of the commercial products (reduced price sales, product giveaways for impoverished patients, and the like).

In its draft policy, CIRM has a provision similar to what Professor Merges describes; §100306(h) directs grantee organizations to take administrative action to modify or terminate license rights where necessary. Professor Merges argues, however, that CIRM should additionally expressly reserve the right to revoke or modify licenses to prevent egregiously unfair practices of licensees; we anticipate that, in certain circumstances,

CIRM, as the funding agency, may be in a better position than the grantee to make such determinations.

4. We suggest that CIRM consider being more directive about its copyright policy.

Copyright is not covered by Bayh-Dole so consistency is not a main concern for CIRM but large quantities of data and informational works will be generated as a consequence of CIRM funding and, at the moment, CIRM's proposals provide little more than hortatory statements. Given that databases, bioinformatics, software tools, and research articles are protected by copyright, CIRM has an opportunity to set an example for other states, and indeed for the US, in setting a forward-looking copyright policy for government funded research. The goal should be to achieve the widest, fastest possible dissemination of knowledge consistent with quality control; this goal can be achieved by providing more specific guidance to grantees on copyright issues. Our suggestions are as follows:

First, university researchers should be able to choose whether to assert copyright in the products of their CIRM-funded research; indeed, they are in the best position to decide when copyright is appropriate. However, they should be encouraged to put materials in the public domain insofar as this will promote rapid and widespread dissemination.

Second, CIRM should require researchers to deposit a copy of their research articles/publications in an open access digital library.⁴ In its "Initial Statement of Reasons," CIRM states, with respect to §100303 – Publication Requirements, that its policy "mandates that results and accomplishments of the activities it funds be made available to the public." We agree with this policy but are not convinced that the pertinent CIRM regulation goes far enough to ensure that result. Too often, publishers of scientific and technical articles insist on transfers of copyright as a condition of publication, and exercise strict controls over access to the published literature.

⁴ For additional support of this principle, see Senators Cornyn and Lieberman's "Federal Research Public Access Act of 2006." <http://www.taxpayeraccess.org/frpaa/index.html> (last visited June 19, 2006).

§100303(a) requires grantees to submit to CIRM a 500 word abstract written for the general public and an accompanying biographical sketch to be deposited in a publicly-accessible database. In our view, a 500 word abstract and biological sketch is not an adequate substitute for a final manuscript. Therefore, we suggest that CIRM require final manuscripts produced as a consequence of CIRM-funded research to be deposited in an open-access digital library.

Third, researchers should be strongly encouraged to adopt Creative Commons licenses or take Open Science or similar open-access pledges and publish only in journals that make works available on open-access terms. For example, authors should be permitted to post their articles on their own website or in open-access repositories.

Finally, researchers should be encouraged to deposit data generated as a consequence of CIRM-funding in an open-access database along the lines developed by Jerome H. Reichman and Paul Uhler in their paper, *A Contractually Reconstructed Research Commons for Scientific Data in a Highly Protectionist Intellectual Property Environment*, 66 Law & Contemporary Problems 315-440 (2003).⁵ In that paper, the authors propose that funding agencies and universities develop agreed contractual templates for the regulation of government-funded data in two specific situations: 1) when government-funded, university-generated data are licensed to the private sector, and 2) when such data are made available to other universities for research purposes.⁶ Such contractual templates, it is argued, should “encourage unconditional deposits of research data, to the fullest extent possible, into both centralized repositories and decentralized network structures” and,⁷ as a second-best alternative, the contractual

See Michael B. Eisen & Andy Gass, *Public Access to Public Science: Recommendations for the CIRM's Policies Regarding Grantee-Produced Journal Articles*, 21 Berkeley Tech. L. J. (forthcoming 2006). A draft of this paper is attached as Appendix B.

⁵ The Reichman & Uhler paper can be found at:

[http://www.law.duke.edu/shell/cite.pl?66+Law+&+Contemp.+Probs.+315+\(WinterSpring+2003\)](http://www.law.duke.edu/shell/cite.pl?66+Law+&+Contemp.+Probs.+315+(WinterSpring+2003)) (last visited June 19, 2006).

⁶ See *id.* at 118.

⁷ See *id.* at 113.

templates should “establish a zone of conditionally available data in order to reconstruct and artificially preserve functional equivalents of a public domain.”⁸

As discussed in the Reichman and Uhler paper, and elsewhere, there are several successful open-access models for data exchange already in existence which CIRM could follow. Such examples include the Science Commons, GenBank, and the Worldwide Protein Data Bank.⁹ Furthermore, Creative Commons licenses are examples of contractual templates which have the ability to preserve the functional equivalent of a public domain through employment of both conditional and unconditional terms of use. Encouraging deposition of data generated from CIRM-funded research into open-access databases will promote CIRM’s goal of speedier, more effective dissemination of knowledge; if the data exchange process is regulated through use of carefully designed contractual templates, many of the obstacles facing CIRM in implementing its objectives will be removed.

5. We agree with CIRM’s draft policy concerning Material Transfer Agreements (MTAs).

MTAs are, strictly speaking, not IP agreements. However, they are critically important to effective technology transfer and the optimal functioning of scientific work to advance knowledge, an IP goal. CIRM has wisely followed the NIH’s lead with respect to its MTA policy but we caution it to consider formulating a more comprehensive MTA policy that systematically addresses donor consent issues and public-private partnerships.¹⁰

⁸ See *id.* at 115.

⁹ See Rebecca S. Eisenberg & Arti K. Rai, *Harnessing and Sharing the Benefits of State-Sponsored Research: Intellectual Property Rights and Data Sharing in California’s Stem Cell Initiative*, 21 Berkeley Tech. L. J. (forthcoming 2006). A draft of this paper is attached as Appendix C.

¹⁰ See Sean O’Connor, *The Use of MTAs to Control Commercialization of Stem Cell Diagnostics and Therapeutics*, 21 Berkeley Tech. L. J. (forthcoming 2006). A draft of this paper is attached as Appendix D.

ABOUT THE CONFERENCE HOSTS:

The Berkeley Center for Law and Technology

The Berkeley Center for Law, Business and the Economy

**California's Stem Cell Initiative:
Confronting the Legal and
Policy Challenges**
University of California, Berkeley
Boalt Hall School of Law
Room 365
Berkeley, CA 94720-7200

The Berkeley Technology Law Journal

The Travers Program on Ethics and Government Accountability

**APPENDIX A: STEM CELL
CONFERENCE PROGRAM**

(stem cell research)

(intellectual property rights)

(recruitment)

(comparative policies)

(bioethics)

CALIF RNIA'S STEM CELL INITIATIVE
CONFRONTING THE LEGAL & POLICY CHALLENGES
March 2 - 4, 2006

LOCATION Boalt Hall School of Law - University of Calif, Berkeley
WEB SITE www.law.berkeley.edu/bol/stemcell/

Most scientists concur that human embryonic stem cell research holds considerable promise for advancing human health. In 2004, California voters endorsed a bold initiative (Proposition 71) to fund stem cell research by the issuance of \$3 billion in bonds, which will be allocated over a 10 year period to researchers.

However, foundational legal and policy issues remain to be resolved — intellectual property rights, biomedical ethics, how (and whether) the state of California should expect to recoup its \$3 billion investment, to name just a few. This conference will provide insights and recommendations from thought leaders to enable California's bold initiative to be successful.

These are among the issues that will be addressed at this tenth annual symposium, co-sponsored by Boalt Hall's Berkeley Center for Law and Technology; the Berkeley Center for Law, Business and the Economy; the Berkeley Technology Law Journal; and UC Berkeley's Travers Program on Ethics and Government Accountability.

SCHEDULE

1:00 - 4:30 PM

TUTORIAL: THE BASIC SCIENCE OF HUMAN EMBRYONIC STEM CELL RESEARCH, AND SOME FOUNDATIONAL LEGAL AND BIOETHICAL ISSUES

Two experts will conduct this tutorial on some of the basic scientific principles and legal and bioethical issues underlying human embryonic stem cell research.

Pilar Ossorio '97 (University of Wisconsin at Madison Law School - Visiting at Boalt Hall School of Law, UC Berkeley)
Michael Shelsanski M.D., Ph.D. (Columbia University)

REGISTRATION AND CONTINENTAL BREAKFAST

8:00 - 8:45 AM

WELCOMING ADDRESS BY BOALT HALL'S

DEAN CHRISTOPHER EDLEY

9:00 - 10:30 AM

GETTING INTELLECTUAL PROPERTY RIGHTS RIGHT: WHAT MODEL SHOULD BE ADOPTED?

It has been 25 years since the adoption of Bayh-Dole, which provides the patent ownership and licensing scheme for federally-funded research. California now has the opportunity to evaluate this approach and other models for inventions resulting from state-funded research. What is the most effective means to induce investment in and commercialization of promising therapeutics while still protecting the public interest?

Moderator: Elizabeth A. Howard (Orrick, Herrington & Sutcliffe LLP)
Merrill Goozner (Integrity in Science Project Director, Center for Science in the Public Interest)
Robert P. Merges (BCLT and Boalt Hall School of Law, UC Berkeley) *
David Mowery (Haas School of Business, UC Berkeley)
Marjorie Shultz '76 (Boalt Hall School of Law, UC Berkeley)

10:30 - 10:45 AM

BREAK

10:45 - 12:00 PM

CONSENT, COMMODIFICATION AND CONTROL

Human eggs, cells and tissue are the foundation of stem cell research. How can donors be protected? What is the best way to ensure appropriate donor consent? Should donors have residual control rights over their eggs, tissue and cells? Is there a danger of market considerations overtaking issues of human and personal importance?

Moderator: Susan Nicholson (Ropes & Gray LLP)
Lori Andrews (Chicago-Kent College of Law)
Sean O'Connor (University of Washington)
Radhika Rao (UC Hastings College of the Law)
David Winickoff (College of Natural Resources, UC Berkeley) *

12:00 - 2:00 PM

LUNCH AND PANEL PRESENTATION AT THE INTERNATIONAL HOUSE KEEPING STEM CELL RESEARCH ON TRACK: BALANCING THE INTERESTS

What are the roles of the different constituencies - the public, patients, government, researchers, and industry - in decision making? Can these interests be balanced? How can the development of cures proceed and the public interest best be served?

Moderator: David Ewing Duncan (Founder and Editorial Director, BioAgenda)
David Gollub (President & CEO, California Healthcare Institute)
Assemblymember Dave Jones (Chair, Judiciary Committee, California State Assembly)
Senator Deborah Ortiz (Health & Human Services Committee Chair, California Senate)
Ed Penhoet (Independent Citizens' Oversight Committee and Vice-Chair, California Institute for Regenerative Medicine)
Joan Samuelson '77 (Independent Citizens' Oversight Committee)

2:00 - 3:30 PM

HOW CAN THE STATE RECOUP ITS INVESTMENT (OR SHOULD IT?)

To finance stem cell research, the state will issue \$3 billion in GO bonds. California is already operating with a massive deficit. Should mechanisms be put in place to pay back the State? If so, what form should this take - a royalty stream, an increased tax base? What are the implications for investment and innovation? What are the prospects for reduced costs in public health care? Or should the payback be the advancement of science and human health?

Moderator: John Wetherell (Pillsbury Winthrop Shaw Pittman LLP)
Richard Gilbert (Department of Economics, UC Berkeley) *
Michael D. Goldberg (General Partner, MDV)
Perry Israel (Partner, Orrick, Herrington & Sutcliffe LLP)
Theodore R. Marmor (School of Management, Yale University)
Roger Noll (Stanford Economics Department, Stanford University) *
Jean Ross (California Budget Project)

3:30 - 3:45 PM

BREAK

3:45 - 5:15 PM

THE IMPLICATIONS FOR HEALTH CARE: LEARNING FROM WHAT IS AND SHAPING WHAT WILL BE

What can we learn from past large scale health care projects? How do we know when it's appropriate to conduct clinical trials? Can the ultimate cures and benefits be equitably distributed? Which diseases should be tackled first? What are the implications for affordability of and access to potential cures?

Moderator: Ken Taymor (MBV Law Firm)
Dana Goldman (Director of Health Economics, The RAND Corporation)
Bernard Lo (Director of CAPS Ethics Core, UCSF)
Jeff Sheehy (Independent Citizens' Oversight Committee)
Charles Thompson (Gender Studies and Rhetoric, UC Berkeley)

5:30 - 7:00 PM

RECEPTION HELD AT THE BERKELEY ART MUSEUM

8:00 - 9:00 AM

REGISTRATION AND CONTINENTAL BREAKFAST

9:00 - 10:30 AM

ON THE OWNERSHIP OF DATA - COPYRIGHT, PUBLIC DOMAIN OR OPEN SOURCE?

Just as significant as patent policy is the ownership policy for databases, data, bioinformatics software, and research articles. How can innovation be encouraged in this arena while still protecting the public interest? Which ownership scheme will best advance the science?

Moderator: **Robert Sloss** (Farella Braun & Martel LLP)

Michael Eisen (Lawrence Berkeley National Laboratory, UC Berkeley)

Rebecca Eisenberg (University of Michigan Law School)

Stephen Maurer (Goldman School of Public Policy, UC Berkeley)

Art Rai (Duke University Law School)

10:30 - 10:45 AM

BREAK

10:45 - 12:15 PM

THE COMPARATIVE CONTEXT: NATIONAL AND INTERNATIONAL APPROACHES TO STEM CELL POLICY

Other jurisdictions have faced or are facing these same issues. What can we learn from their successes and failures? Should we do things differently?

Moderator: **Sergio Garcia** (Fenwick & West LLP)

R. Alta Charo (University of Wisconsin at Madison Law School)

visiting at Boalt Hall School of Law, UC Berkeley)

Madred K. Cho (Stanford University Center for Bioethical Ethics)

Rosario Isasi (Centre de Recherche en Droit Public, Université de Montréal)

Christopher Scott (Stanford Stem Cell Center)

12:15 - 2:00 PM

**LUNCH AND PANEL PRESENTATION AT THE BANCROFT HOTEL
THE POLITICAL PROCESS AND STEM CELL RESEARCH:
HOW DID WE GET HERE AND WHAT CAN WE LEARN?**

Organized by the Travers Ethics Program at UC Berkeley

The debate surrounding stem cell research in general, and Prop 71 in particular, raises a number of questions about the role of democratic control in scientific, legal and policy decisions. Should there be democratic control and if so how should that be facilitated? How can we have intelligent public debates about highly technical issues like stem cell research? What have we learned from Prop 71 about the role of democratic debate that might inform future initiatives? Are initiatives which by definition are structured to appeal to the public, the best ones?

Moderator: **Robert Price** (Associate Vice Chancellor for Research and

Professor of Political Science, UC Berkeley)

Marcy Darnovsky (Center for Genetics and Society)

Kath E. Hanna (Science and Health Policy Consultant)

Theodore R. Marmor (School of Management, Yale University)

Joanna Weinberg (Institute for Health and Aging, UCSF)

APPENDIX B:

Public Access to Public Science: Recommendations for the CIRM's Policies Regarding Grantee-Produced Journal Articles

Michael B. Eisen, Ph.D.
Department of Molecular and Cell Biology
UC Berkeley

Andy Gass
Boalt Hall Class of 2008
UC Berkeley

Competing Interests Statement: Michael Eisen is a co-founder and member of the Board of Directors of the Public Library of Science, a non-profit organization that publishes open-access biomedical journals. Andy Gass is a former employee of the Public Library of Science.

While the public's attention has been focused on a number of high-profile controversies presented by the prospect of a taxpayer-funded institute for stem cell research, several more arcane—but nevertheless important—matters have largely escaped the notice of the community activist groups, the town-hall meeting attendees, and the reporters covering the California Institute for Regenerative Medicine [CIRM]. One such question is who will own the rights to the peer-reviewed journal articles written by CIRM-funded researchers—an open issue whose resolution will substantially determine how accessible those articles will be online for other scientists, for the media, for students, and for the justifiably curious public. In this brief article, we argue that in the context of stem cell research, a policy arena rife with seemingly intractable disputes that implicate deeply held and conflicting moral intuitions, one of the few questions that has a relatively straightforward answer is whether policymakers should require that publications arising from CIRM-funded research be freely accessible online. They undoubtedly should. The benefits of a well-crafted plan in this area would be tremendous, and the downsides would be trivial. The primary argument against such a policy—that scientists would decline to apply for CIRM funding if it came with an “open access” requirement—is simply implausible.

I. The imperatives for and practical possibility of open access to CIRM-funded journal articles

Why should the CIRM require that articles produced by its funded investigators be free online? Look ahead 3 or 4 years from now, as the first round of projects funded by the institute will be completed. While we can hope that this research will be producing powerful new treatments for diseases from diabetes to Parkinson's, such rapid progress is unlikely to have occurred. Rather than generating cures initially, CIRM-funded projects will be generating *knowledge* about the basic biology of stem cells—how they behave in the lab and in the clinic—and about prospective applications that do and do not show promise. The public, eager to see the highly touted potential of stem cell research

fulfilled, and interested to know if its first billion dollars was well spent, will be paying particular attention and will undoubtedly scrutinize these projects in great detail. But, if the prevailing practices of the scientific community are allowed to persist, the sole tangible product of this publicly supported scientific research will be too expensive for the public to access. And for no particularly good reason.

A. Scientific publishing: background and overview

Scientific projects are not finished when the last experiment is done; they are truly complete only when the results are available for others to scrutinize and build on in their own research. Scientists conduct this communication and correspondence with their colleagues by publishing papers—replete with details of the methods used, the results obtained and conclusions reached—in peer-reviewed journals. These journals are the lifeblood of the scientific community and have been since the 17th century, when the Royal Society in London began publishing accounts of experiments and lectures for farflung members and interested laymen who could not attend the regular meetings. There are now many thousands of scientific journals, and their collective contents are one of humanity's greatest creations—the accumulated ideas and discoveries of tens of thousands of scientists, living and dead, who have dedicated themselves to figuring out how the world works. Today, virtually all of these journals are online, and anyone who logs onto the computer network at a major American university has instant access to the latest discoveries in fields ranging from quantum mechanics to astrophysics to, indeed, stem cell research.

Outside of research institutions, however, access to the scientific literature is extremely limited. How can, and why do, publishers of scientific journals erect barriers to prevent the public from accessing their contents? The answer lies in the curious fact that the only permanent record of the scientific process is owned and controlled not by the scientific community, or the public that largely funds its work, but rather by the publishers of scientific journals—who first require as a condition of publication that authors transfer the copyrights in their works, and then wield those rights to charge scientists and their institutions steep fees to access their journals.¹¹

While this state of affairs may seem sensible from the perspective of those publishers, the relatively singular system by which scientific research papers come into being renders the prevailing model of disseminating scientific knowledge decidedly disadvantageous for the institutions that produce the work, then buy it back. Consider the relative contributions of different groups to the production of a finished scientific paper. There are the scientists, who did the experiments and submitted their work for publication, with no expectation of remuneration. Then there are the volunteer peer-reviewers—other scientists—who carefully pored over the details of the paper, to make sure the methods were sound, the data valid and the conclusions warranted by the results. Finally there are the sponsors—usually the government or other public institutions—who paid for the

¹¹ In 2002-2003, for example, the University of California paid \$8 million for online access *just to scientific journals published by Reed-Elsevier*—a figure that represented fully one-sixth of UC's materials budget that year. See http://www.lib.berkeley.edu/Collections/elsevier_case_study.html.

research and the salaries of the experimenters. The publisher does something too: it manages the editing and peer-review process, oversees production, and posts the completed articles on the web. But to reward this modest contribution to the process with permanent control of the finished product is at best sub-optimal from the perspective of most of the other stakeholders, and at worst simply absurd.¹²

Why have scientists and their institutions allowed such a system to develop and take root? Until recently, the cheapest and most efficient way to distribute scientific knowledge was by printing journals and delivering them through the mail, and the costs of publishing a scientific journal were mostly in producing and distributing printed pages. Since these costs naturally scaled with the number of readers, a subscription-based business model, in which publishers charged for each copy they distributed, made good economic sense, and was reasonably efficient and fair to readers, to boot. To capitalize on their front-end investments in paper, printing and postage, journals requested that scientists grant them the exclusive right to publish their work, and scientists—unable to publish and distribute works on their own—were happy to comply.

However, with the rise of the internet, the trade-offs embodied in this system no longer benefit the producers and users of scientific articles to the same degree. Today, the cheapest and most useful way to distribute published scientific work is on the internet. When research articles are published online, all the costs intrinsic to the publication process arise from producing the initial peer-reviewed, edited and formatted copy of each work. With printing costs eliminated, and distribution infinitesimally cheap, the costs of publication are now independent of the number of readers.

Despite this fundamental pragmatic change, most scientific publishers persist in charging individuals and institutions for the right to access the papers they have published. Setting aside for a moment the question whether this system remains desirable or not in the end, there is no question that its prevalence is a vestige of a time when the economics of the publishing process were very different than they are today. And it hardly seems radical to suggest that, if the stakeholders in science were to devise *de novo* a system to pay for the peer-review and online publication of research papers, they might very well not opt for one in which the final product was accessible only to people or institutions willing to pay annual or per-download fees.

For subscription charges and other access fees are now, in some respects, an obstacle to the optimal use of scientific knowledge. They inhibit scientific and medical progress by curtailing the free flow of information upon which research depends; they prevent the development of creative new ways to sort through and use the information contained in

¹² One might, for example, compare the publisher to a midwife. Midwives play an important role in the birth of a child—just as publishers play an important role in the final step of the scientific process. But no midwife would claim that his or her contribution should be rewarded with ownership of the baby. Yet, in a sense, this is precisely what happens in scientific publishing; it's as if midwives claimed ownership of babies and charged parents an annual fee to visit their child.

the literature; and they deny the public access to the treasury of scientific knowledge it has paid trillions of dollars to create. Insofar, then, as there exists a way to publish scientific research articles sustainably and *without* fees for access, that alternative system inherently offers numerous advantages over the traditional one.

B. Scientific publishing: alternative trends and recent developments

Over sixty percent of internet users have searched for medical information online—more than have downloaded music or salacious images of movie stars.¹³ But while Google searches for any disease or symptom return a bevy of information, ranging from the useful and informative to the dangerous and quackish, they rarely turn up the careful, peer-reviewed studies published in major medical journals that contain the most up-to-date and useful medical knowledge available.

The institutions that fund scientific research are gradually becoming aware that this is a problem, and are slowly—very slowly—devising solutions. The National Institutes of Health [NIH], for example, promulgated a policy in 2005 requesting that scientists who received research grants from the agency's \$28 billion budget submit their resulting journal articles to an online, free-to-access library called PubMed Central.¹⁴ Because compliance is not mandatory, however, and because individual scientists typically have minimal or indirect incentives from self-interest to make their own articles free online, authors' participation in the NIH program has been negligible.¹⁵ The Wellcome Trust, the United Kingdom's largest private funder of biomedical research, has gone a step further. Starting October 1 of this year, all journal articles resulting from the £400 million that the charity disperses annually in research grants will be deposited in PubMed Central, by rule.¹⁶

Faced with the prospect of funder-imposed requirements that journal articles be made free online, scientific publishers have divided into two camps. The first embraces the change, and has begun to adopt business models that are consistent with providing unfettered access to journal contents. Those models typically entail an upfront fee, paid from researchers' grants or from centralized pools of money that funders have made available, to cover the publisher's costs of overseeing peer-review and preparing accepted articles for publication.¹⁷ The Wellcome Trust has estimated that such fees, if paid for all

¹³ Pew Internet and American Life Project (2003) Internet health resources. Available: http://www.pewinternet.org/pdfs/pip_health_report_july_2003.pdf.

¹⁴ PubMed Central, which contains the full texts of scientific papers, is distinct from PubMed, which contains the abstracts of scientific papers.

¹⁵ National Institutes of Health "Report on the NIH Public Access Policy," February 1, 2006. Available at <http://publicaccess.nih.gov/news.htm>. It is worth noting, however, that support is high among prominent scientists for mandatory deposition of NIH-funded articles in PubMed Central. See e.g. "An Open Letter to the US Congress Signed by 25 Nobel Laureates (advocating a requirement that taxpayer-funded research articles be made freely available to the public). Available at www.fas.org/sgp/news/2004/08/nobel082604.pdf

¹⁶ See <http://www.wellcome.ac.uk/node3302.html>.

¹⁷ See e.g. *Proceedings of the National Academy of Sciences* (whose policy is described in "An open access option for PNAS," available at <http://www.pnas.org/cgi/content/full/101/23/8509>).

the journal articles its grantees produce, would amount to between one and two percent of the cost of conducting the research reported in the papers.¹⁸

The second camp of publishers, by contrast, has resisted calls to make the scientific literature free online. The principal grounds for their obstruction has been purely financial, as journals like *Science* have suggested that funding agencies simply would not be willing to pay upfront what it costs to publish a research article in a selective forum.¹⁹ Independent estimates, however, indicate that such claims of economic impracticality tend to be wildly exaggerated.²⁰

An alternative reason for resistance has been a more overtly misguided concern over potential misuses of articles to which publishers hold only some, rather than all, rights. The *New England Journal of Medicine* [NEJM], for example, has cautioned of the following danger: if a funder of research prohibits its grantees from transferring the full rights to their articles to NEJM, then the paltry non-exclusive rights the journal would acquire would effectively “allow third parties to selectively use the materials in scholarly articles for commercial gain.”²¹ Not only does such concern betray a profound misunderstanding of copyright law—which of course bestows a thin layer of protection on technical works, in the first place, and which allows fair uses of portions of copyrighted research articles, in any event—but it fails to support the asserted conclusion (that copyrights must always be transferred in full) even on its own terms. For NEJM, along with every other publisher of biomedical journals, routinely publishes articles whose exclusive rights it does not hold: those written by scientists not merely *funded* by NIH, but *employed* there, whose works automatically enter the public domain, by virtue of 17 U.S.C. § 105.²² To date, there has not been a single report of misleading or inappropriate use of any article produced by researchers in the two dozen NIH institutes and centers, despite that all such articles are wholly unprotected by copyright.²³

The significance of the copyright-transfer exception that publishers routinely make for NIH intramural researchers is often overlooked in discussions of funder-imposed public access requirements. It demonstrates, however, that virtually all journals are willing publish good science, regardless of whether the authors of an article are for some reason prohibited from assigning rights in the work to their publisher.

¹⁸ “Paying to Free Science: Costs of Publication as Costs of Research,” Andy Gass. *Serials Review* Vol. 31, Number 2, 2005, at p. 105. Freely available at <http://www.plos.org/oa/plosoa.html>.

¹⁹ See “The Promise and Peril of Open Access,” *Chronicle of Higher Education*, January 30, 2004 (including an estimate by the American Association for the Advancement of Science that it would have to charge \$10,000 per paper to make its articles free online and maintain the revenue it derives from subscriptions). Available at <http://chronicle.com/free/v50/i21/21a01001.htm>.

²⁰ “Costs and Business Models in Scientific Research Publishing,” A Report Commissioned by the Wellcome Trust, at p. 3 (finding that the per-article cost to publish in a high quality, subscription-based scientific journal is around \$2750). Available at http://www.wellcome.ac.uk/doc_WTD003185.html.

²¹ “Public Access to Biomedical Research,” Jeffrey Drazen and Gregory Curfman, *NEJM* Volume 351:1343, September 23, 2004. Available at <http://content.nejm.org/cgi/content/full/351/13/1343>.

²² “Copyright protection under this title is not available for any work of the United States Government. . .”

²³ It also bears mention that scientific journals whose entire contents are governed by permissive Creative Commons licenses, such as those published by the organization The Public Library of Science, have reported no ill effects of such liberal copyright terms in their concededly brief histories of operation.

II. Policy recommendations and final comments

Proposition 71, along with the institute it funded, is—if nothing else—a grand experiment in direct public support for biomedical research, and one whose successes and failures will impact not only stem cell research but also the broader relationship between science and the public. In order to ensure that the public is fully informed about the results of CIRM-funded research, and in order to share as widely as possible the benefits of the knowledge that such research produces, the CIRM should adopt the following policies regarding the journal articles that result from its grantees' investigations:

1. Like works produced by NIH intramural researchers, the articles should not be protected by copyright, and should instead be dedicated to the public domain, by rule, in order to allow the public to make creative use of the works in databases, for patient advocacy purposes, in educational settings, and for other ends.
2. As a condition of accepting CIRM funds, grantees should be required to deposit with PubMed Central [PMC] either the final manuscripts or the published versions of all articles that result from their CIRM-funded work, for posting in PMC immediately upon publication in the journals in which they appear.
3. The CIRM should make available a standing fund from which grantees can draw money to pay the reasonable costs of publication in open-access journals which request such fees.

At the Boalt Hall conference that spawned this essay and the other works in this volume, several knowledgeable and influential legal scholars expressed concerns that imposing conditions such as these on grants would cause scientists to turn elsewhere for funds to do stem cell research with fewer strings attached—in other words, that requiring open access to CIRM-funded journal articles would scare the best scientists off. Little empirical data is available, it seems, regarding the influence of grantor result-sharing requirements on scientists' willingness to accept funds burdened with such conditions. For what little it may be worth, however, the fear that scientists might be driven away strikes us as entirely baseless. Few scientists tend to be concerned that their funders require them to be too *open* with the results of their work (although it is undoubtedly the case that some scientists refuse grants that would require them *not* to publicize some findings). Furthermore, even for those practicing stem cell researchers who might, all else being equal, object to our proposed conditions, the sad reality is that funds for stem cell research, at least in this country, are relatively hard to come by. In other words, it seems very unlikely that a qualified scientist would turn down a CIRM grant because the articles she produced would enter the public domain and be made free online.

How would scientific journals react to this proposed policy? If their treatment of NIH intramural authors is any indication, then the journals would accept CIRM-funded authors with open arms, despite the scientists' inability to transfer rights in their articles to their publishers. In the event that some journals did object, and refused to publish

CIRM-funded articles, the reality would be that the only stakeholder to end up worse-off would be those journals, themselves. The public would still have access to the identical scientific paper, but published in a CIRM-friendly journal (such as the many peer-reviewed open-access venues which thrive on the front-end payment model described above). The institutions that evaluate the scientist/author's work (for the purposes of tenure, promotion, and future grants) would be aware that some journals do not publish CIRM-funded work, and would adapt their metrics of evaluation accordingly. Certainly, the publication that refused the article would suffer for excluding an otherwise worthy contribution to the scientific literature for reasons unrelated to its intellectual merit—but at the end of the day, as between the bottom line of a subscription-based journal publisher, and the public's interest in access to scientific information, the CIRM policymakers should choose to support the latter.

APPENDIX C:

Harnessing and Sharing the Benefits of State-Sponsored Research: Intellectual Property Rights and Data Sharing in California's Stem Cell Initiative

Rebecca S. Eisenberg & Arti K. Rai

Introduction

The considerable attention that the California Institute for Regenerative Medicine (CIRM) and its Independent Citizens' Oversight Committee (ICOC) have already devoted to framing its intellectual property (IP) policies²⁴ is a sure sign of the growing salience of IP in biomedical research. In its Intellectual Property Policy for Non-Profit Organizations (IPPNPO), CIRM has endorsed a public-spirited "core principle" to "encourage broad dissemination of CIRM-funded intellectual property of all types beyond practices commonly used in 2005 to promote scientific progress."²⁵ At the same time, CIRM acknowledges competing interests that might limit such sharing, including bringing scientific advances to the public via commercialization and providing a financial benefit to the State of California through revenue sharing.²⁶ Indeed, the terms of Proposition 71, the initiative that created CIRM, explicitly direct attention to these competing interests.²⁷

When it comes to balancing competing interests, the devil is in the details. The IPPNPO is richly detailed with respect to patenting, licensing, and the exchange of research materials, generally following evolving standards of "best practices" for federally-funded research articulated in reports emanating from the National Institutes of Health.²⁸ But it barely touches upon details in stating CIRM's expectations with respect to data-sharing.²⁹

In recent years data-sharing has been a recurring focus of struggle within the biomedical research community as improvements in information technology and digital

²⁴ See Calif. Inst. of Regenerative Med., Intellectual Property Policy for Non-profit Organizations, approved by the Independent Citizen's Oversight Committee Feb. 10, 2006 (hereinafter IPPNPO), posted at <<http://www.cirm.ca.gov/policies/pdf/ippnpo.pdf>>. See also Calif. Council on Sci. & Tech., Policy Framework for Intellectual Property Derived from Stem Cell Research in California: Interim Report to the California Legislature, Governor of the State of California, California Institute for Regenerative Medicine (2005).

²⁵ IPPNPO, *supra* at 25.

²⁶ *Id.* at 4-5.

²⁷ Proposition 71, Sec. 3, posted at <<http://www.cirm.ca.gov/prop71/pdf/prop71.pdf>>.

²⁸ See, e.g., Principles and Guidelines for Recipients of NIH Grants and Contracts on Obtaining and Disseminating Biomedical Research Resources, 64 Fed. Reg. 24090 (Dec. 23, 1999), posted at <<http://ott.od.nih.gov/pdfs/64FR72090.pdf>>, cited with approval in IPPNPO at

²⁹ The IPPNPO embraces the lofty aspirations for data-sharing set forth in a series of recent reports from the National Research Council, see, e.g., National Research Council, Reaping the Benefits of Genomic and Proteomic Research: Intellectual Property Rights, Innovation, and Public Health (2006); National Research Council, Sharing Publication-Related Data and Materials: Responsibilities of Authorship in the Life Sciences (2003), cited in IPPNPO, *supra* note at 26-27.

networks have expanded the ways that data can be produced, disseminated, and used.³⁰ Information technology makes it easier to share data in publicly accessible archives that aggregate data from multiple sources. Such sharing and aggregation facilitate observations that would otherwise be impossible. But data disclosure poses a dilemma for scientists. Data have long been the stock in trade for working scientists, lending credibility to their claims while highlighting new questions that are worthy of future research funding. Some disclosure is necessary in order to claim these benefits, but data disclosure may also benefit one's research competitors. Scientists who share their data promptly and freely may find themselves at a competitive disadvantage relative to free riders in the race to make future observations and thereby to earn further recognition and funding. The possibility of commercial gain further raises the competitive stakes. As information technology has advanced, and as commercial interests in biomedical research have grown, this dilemma has become more pronounced.

Data per se are generally considered ineligible for either copyright or patent protection.³¹ As a consequence, the Bayh-Doyle Act,³² which governs patent rights in the results of federally-sponsored research, does not directly address the dissemination of unpatentable data.³³ Meanwhile, the scientific community has sought to clarify its data-sharing norms and to figure out how to implement them.³⁴ One important focus of debate has been the extent of data disclosure that ought to accompany scientific publication.³⁵ Although disclosure of research results is the essence of scientific publications, typically print publications only reveal data in summary form, leaving authors with substantial control over access to the underlying raw data. In an earlier era such summary disclosures may have been the best that could be achieved as a practical matter given scarcities of space associated with print media. But with the growth of the internet and information technology, it is now a simple matter to make vast data sets available over the internet at minimal cost. Yet a recent survey found that less than half of the most frequently cited journals in the life sciences and medicine had policies requiring deposit of data associated with published articles.³⁶

³⁰ See, e.g., National Research Council, *Sharing Publication-Related Data and Materials: Responsibilities of Authorship in the Life Sciences* (Nat'l Acad. Press 2003). See generally National Research Council, *Bits of Power: Issues in Global Access to Scientific Data* (1997).

³¹ For a review of the limits on copyright protection of data with citations to the relevant cases and literature, see J.H. Reichman & Paul F. Uhler, *A Contractually Reconstructed Research Commons for Scientific Data in a Highly Protectionist Intellectual Property Environment*, 66 L. & Contemp. Prob. 315, 336-341 (2003). For a review of the limits on patent protection of data, see U.S. Pat. & Trademark Off., *Interim Guidelines for Examination of Patent Applications for Patent Subject Matter Eligibility* (2005), posted at <<http://www.uspto.gov/web/offices/com/sol/og/2005/week47/patgupa.htm>>.

³² Act of Dec. 12, 1980, Pub. L. No. 96-517, 94 Stat. 3015 (1980) (codified as amended at 35 U.S.C. §§ 200-212).

³³ Although *sui generis* database protection has been enacted in Europe, Council Directive 96/9 of 11 March 1996 on the Legal Protection of Databases, 1996 O.J. (L 77), and proposed in the U.S., it has not yet been passed into law in the U.S. For a review of U.S. database protection proposals from the perspective of the scientific community, see J.H. Reichman & Paul F. Uhler, *Database Protection at the Crossroads: Recent Developments and Their Impact on Science and Technology* Berkeley Tech. L.J. 793 (1999).

³⁴ See, e.g., National Research Council, *Finding the Path: Issues of Access to Research Resources* (1999); National Research Council, *Sharing Publication-Related Data and Materials: Responsibilities of Authorship in the Life Sciences* (Nat'l Acad. Press 2003).

³⁵ See, e.g., National Research Council, *Finding the Path: Issues of Access to Research Resources* (1999); NATIONAL RESEARCH COUNCIL, *SHARING PUBLICATION-RELATED DATA AND MATERIALS: RESPONSIBILITIES OF AUTHORSHIP IN THE LIFE SCIENCES* (Nat'l Acad. Press 2003) (hereinafter *SHARING PUBLICATION-RELATED DATA AND MATERIALS*).

³⁶ *Id.* at 33 Table 2-1.

Debate within the scientific community over the disclosure obligations associated with publication reached a fevered pitch with the publication in the prestigious *Science* magazine of an article announcing the completion of the human genome sequence by scientists at the private firm Celera.³⁷ Although Celera made its human genome sequence available free of charge from its own website, access was restricted along certain dimensions, including quantitative limitations on the amount of data that could be downloaded, a prohibition on redistribution, and additional limitations on commercial users.³⁸ The National Research Council responded by forming a Committee on Responsibilities of Authorship in the Biological Sciences to examine the topic of sharing published data and materials. That Committee issued a report that called upon authors to include in their publications or otherwise make freely available “the data, algorithms, or other information that is central or integral to the publication – that is, whatever is necessary to support the major claims of the paper and would enable one skilled in the art to verify or replicate the claims.”³⁹ The report further indicated that data access terms should allow for cumulative improvement.⁴⁰ In this regard, it specifically condemned the terms of access to the Celera human genome sequence data as “not consistent with the principles laid out in this report,” noting that it permitted only “static access” for purposes of validation and not “dynamic access” for use in further research.⁴¹

Research projects that have as their aim the creation of large data sets over an extended period of time have presented special challenges for the implementation of data-sharing norms. The usual trigger for disclosure in academic research—publication of research results—would not serve as a timely enforcer for release of accumulating data that might not be ripe for publication in a prestigious journal until long after it was generated. A series of international collaborative research efforts in genomics that specifically aim to create community resources for widespread use have prescribed data-sharing policies to override the inclination of scientists to withhold data pending publication.⁴² These efforts have also aimed to defeat patents corresponding to the data, and even on downstream improvements to the data.⁴³

Outside of genomics, NIH has also explored mechanisms of using its leverage as research sponsor to guide the data-sharing practices of its grantees.⁴⁴ In recent years NIH has required researchers applying for more than \$500,000 in funding to submit a plan for

³⁷ J. Craig Venter et al., *The Sequence of the Human Genome*, 291 *SCIENCE* 1304-51 (2001).

³⁸ *Accessing the Celera Human Genome Sequence Data*, posted at <http://www.sciencemag.org/feature/data/announcement/gsp.dtl>.

³⁹ SHARING PUBLICATION-RELATED DATA AND MATERIALS AT 5

⁴⁰ *Id.* at 62.

⁴¹ *Id.* at 48 Box 3-2.

⁴² See, e.g., Summary of principles agreed at the International Strategy Meeting on Human Genome Sequencing, Bermuda, 25th-28th February 1996, <http://www.gene.ucl.ac.uk/hugo/bermuda.htm>; Sharing Data from Large-Scale Biological Research Projects: A System of Tripartite Responsibility, Report of a meeting organized by the Wellcome Trust and held on 14-15 January 2003 at Fort Lauderdale, USA, <http://www.wellcome.ac.uk/assets/wtd003207.pdf>.

⁴³ See International HapMap Project, <http://www.hapmap.org/cgi-perl/registration>

⁴⁴ See Final NIH Statement on Sharing Research Data, Feb. 26, 2003, at <http://grants1.nih.gov/grants/guide/notice-files/NOT-OD-03-032.html>.

data sharing.⁴⁵ NIH cites a compelling list of arguments in support of such sharing, including reinforcing open scientific inquiry, facilitating new research, encouraging diversity of analysis and opinions, enabling the exploration of topics not envisioned by the original investigators, and permitting the creation of new data sets that combine data from different sources. The policy stops short of mandating data-sharing, however, acknowledging competing interests in “protecting confidential and proprietary data.”⁴⁶

These initiatives provide useful benchmarks for CIRM to consider in formulating its own approach to data-sharing. At the same time, they do not necessarily constrain CIRM. Although even a relatively large state-sponsored research initiative such as CIRM may be constrained as a practical matter in setting its patent policies by the reality that other publicly-sponsored institutions conducting stem cell research are using their discretion under Bayh-Dole to pursue patents,⁴⁷ CIRM is less constrained with respect to data-sharing policy. This is because of the relative lack of binding legal authority concerning rights in data and because of the great variability in policy and practice concerning data-sharing within the biomedical research community. Indeed, CIRM may be well-positioned by virtue of the scale of its operation and the scarcity of federal funding for stem cell research to take a leadership role in setting the terms for data-sharing in this context. Nonetheless, it is important to recognize that CIRM is not the only sponsor of stem cell research, and it needs to be cognizant of the IP and data strategies of other institutions involved in stem cell research and other biomedical research in the public and private sectors as it sets its own course.

This article examines some of these strategies and considers their implications for CIRM. We begin by considering how IP law affects data-sharing. We then consider the agendas that guide the IP policies and strategies of federal, state, and private research sponsors. With this background, we discuss four specific sets of questions that public sponsors of data-rich research, including CIRM, are likely to confront.

The Role of Patent Law in Data-Sharing

Neither copyright nor patent law offers federal statutory protection for data as such. Indeed, both copyright law and patent law treat the informational content of writings and inventions as a spillover benefit for the public, while limiting the exclusionary rights of creators to something else - an original expression in the case of copyright,⁴⁸ and a product or process in the case of patent.⁴⁹ Both legal regimes

⁴⁵ NIH Data Sharing Policy and Implementation Guidance (March 5, 2003), posted at <http://grants.nih.gov/grants/policy/data_sharing/data_sharing_guidance.htm>.

⁴⁶ *Id.* at 1.

⁴⁷ The most significant university patents are held by the Wisconsin Alumni Research Foundation (“WARF”). WARF holds broad patents on both embryonic stem cell lines generally and human embryonic stem cell lines in particular.

⁴⁸ *Cf. Feist Publications v. Rural Telephone Service Co.*, holding that an alphabetized list of names and phone numbers lacked the minimum originality necessary for copyright protection, even though considerable effort may have gone into creating it.

nonetheless tend to promote information dissemination by offering exclusive rights that survive even after disclosure.

By requiring public disclosure of information about an invention while limiting the exclusive rights to the inventions defined in claims, patent law not only fails to protect information, but actually pushes it into the public domain as a spillover. But although the information disclosed in a patent application is publicly disclosed, the exclusionary rights from the patent might still protect the patent owner from some unauthorized uses of the information that involve infringing the patent on the invention. For example, if an inventor discloses how to make and use a new mousetrap in a patent application, and a patent issues with claims drawn to the mousetrap, anyone who follows the directions in the disclosure to make and use the mousetrap would be liable for infringement. In other words, although patent law causes information about how to make and use inventions to become publicly available, patent rights effectively limit its use.

Patent law concerning the scope of the “prior art” for purposes of evaluating the patentability of inventions has complex effects on incentives for information disclosure. Those who hope to file patent applications may be inclined to defer disclosure until after their application filing dates by rules that count all publicly available information, including the inventor’s own disclosures, as prior art.⁵⁰ On the other hand, those who wish to defeat potential patent applications by their scientific or commercial rivals may disclose information in the hope of creating more prior art.⁵¹ The creation of patent-defeating prior art appears to have played a role in the development of disclosure rules for some large-scale biological resource projects.⁵²

On one reading, the failure to protect information under patent law and copyright law shows that information gets no respect. This is the sense that emerges from reading

⁴⁹ Patentable subject matter is limited by statute to any new and useful process, machine, manufacture, or composition of matter, 35 U.S.C. § 101, all generally understood to be distinct from data or information. The subject matter boundaries of the patent system have been falling away in recent judicial decisions in the face of creative claiming strategies for new technologies, particularly information technology. See, e.g., *State Street Bank & Trust v. Signature Financial Group*, 149 F.3d 1368 (Fed. Cir. 1998), *cert. denied*, 119 S. Ct. 851 (1999); *AT&T Corp. v. Excel Communications, Inc.*, 172 F.3d 1352 (1999). On the other hand, the Supreme Court recently granted certiorari in the case of *Laboratory Corporation of America Holdings v. Metabolite Laboratories Inc.*, 370 F.3d 1354 (Fed. Cir. 2004), *cert. granted*, 126 S. Ct. 543 (2005), *vacated, reconsidered, and cert. granted*, 126 S. Ct. 601 (2005), limiting the scope of its review to the question of patentable subject matter. This decision could potentially alter the trend toward more expansive patent eligibility.

⁵⁰ 35 U.S.C. §§ 102, 103. An inventor’s own disclosures will not defeat the novelty of an invention under U.S. law because they do not show prior invention, knowledge or use by another prior to the invention date, 35 U.S.C. §§ 102(a), (g), but they may nonetheless give rise to a “statutory bar” against a patent if the disclosure occurred more than a year before the inventor’s filing date. 35 U.S.C. §§ 102(b).

⁵¹ Gideon Parchomovsky, *Publish or Perish*, 98 Mich. L. Rev. 926 (2000); Douglas Lichtman, Kate Kraus & Scott Baker, *Strategic Disclosure in the Patent System*, 53 Vanderbilt L. Rev. 2175 (2000); Rebecca S. Eisenberg, *The Promise and Perils of Strategic Publication to Create Prior Art: A Response to Professor Parchomovsky*, 98 Mich. L. Rev. 2358 (2000).

⁵² See *infra*.

copyright cases like *Feist*,⁵³ and forms the basis of an argument for database protection. In this story copyright law treats information as a mere byproduct of efforts that deserve protection only insofar as they yield something else that is more creative. Contemporary critics charge that IP law has failed to appreciate the importance of information as an artifact of human ingenuity with value in its own right, and as this value grows and becomes more vulnerable to misappropriation with expanding capabilities of IT, this limitation on legal rights is becoming more anomalous.⁵⁴

From another perspective, the failure to protect information may reflect a reverence for information as something that is too important to society to permit it to be monopolized. This is the sense that emerges from reading cases about disclosure in the patent system, in which courts treat the informational content of patent applications as the public's *quid pro quo* that justifies the issuance of patents.⁵⁵ In this story disclosure of unprotected information is not an incidental byproduct of a process that aims to motivate something more worthwhile, but the whole point of the patent system. In other words, we promote disclosure of precious information by rewarding disclosure with exclusionary rights in something else.

Strategic Considerations of Sponsors in Data-Sharing

The absence of federal IP rights in data is by no means a guarantee that data will be shared freely in the public domain. Quite the contrary, in the absence of statutory protection like a patent or copyright that survives beyond disclosure, a standard commercial strategy for preserving the value of data and databases has been secrecy, or more accurately, restricted access. Some valuable databases are used only internally

⁵³ "The sine qua non of copyright is originality. To qualify for copyright protection, a work must be original to the author. [] Original, as the term is used in copyright, means only that the work was independently created by the author (as opposed to copied from other works), and that it possesses at least some minimal degree of creativity. [] To be sure, the requisite level of creativity is extremely low; even a slight amount will suffice. The vast majority of works make the grade quite easily, as they possess some creative spark, "no matter how crude, humble or obvious" it might be. [] ... [F]acts do not owe their origin to an act of authorship. The distinction is one between creation and discovery: the first person to find and report a particular fact has not created the fact; he or she has merely discovered its existence. ... [O]ne who discovers a fact is not its "maker" or "originator." [] "The discoverer merely finds and records." 499 U.S. 340, 345-57 (1991).

⁵⁴ See, e.g., Jane C. Ginsburg, *U.S. Initiatives to Protect Works of Low Authorship*, in R. Dreyfuss et al., eds, *Expanding the Boundaries of Intellectual Property: Innovation Policy for the Knowledge Society* (Oxford 2001)

⁵⁵ See, e.g., *Kewanee Oil v. Bicron*, 416 U.S. 470, 481 (1974) ("When a patent is granted and the information contained in it is circulated to the general public and those especially skilled in the trade, such additions to the general store of knowledge are of such importance to the public weal that the Federal Government is willing to pay the high price of 17 years of exclusive use for its disclosure, which disclosure, it is assumed, will stimulate ideas and the eventual development of further significant advances in the art."); *Bonito Boats v. Thundercraft*, 489 U.S. 141, 151 (1989) ("[T]he ultimate goal of the patent system is to bring new ideas and technologies into the public domain through disclosure. State law protection for ideas and designs whose disclosure has already been induced by market rewards may conflict with the very purpose of the patent laws by decreasing the range of ideas available as the building blocks of further innovation.") *United States v. Dubilier Condenser Corp.* 289 U.S. 178, 186-87 (1933) ("[The inventor] may keep his invention secret and reap its fruits indefinitely. In consideration of its disclosure and the consequent benefit to the community, the patent is granted.").

within a firm or made available only to paying subscribers under the terms of database access agreements; these may be protectible as trade secrets. At a minimum, they are protected under the law of contracts. Even without having to go to court to enforce legal rights, database owners may exercise considerable control through restricted access to the contents of databases made available over the internet in client-server mode.

These strategies allow database owners to exclude free riders, and perhaps thereby to capture enough value to justify creating the database. They are wasteful from a social perspective because they restrict dissemination of information that would have greater social value if it were made more broadly available, and that could be made freely available at minimal additional cost. Restricting access may lead to socially wasteful duplication of effort as competitors have to recreate similar databases for their own use. It also makes it more difficult to aggregate data from multiple sources to create more comprehensive databases. Nonetheless, trade secrecy has an important role to play in encouraging firms to invest in the creation of databases.

The case for trade secrecy is weaker for information generated at public expense. Public funding mitigates concerns about the adequacy of incentives to generate the information, and makes the social waste inherent in secrecy more troubling. The mission of public sponsors to advance science is likely to be better served by broad dissemination. Data disclosure can also provide a valuable check on fraudulent research claims, a risk that has regrettably become salient in the recent experience of stem cell research.⁵⁶ Data disclosure also provides a check against overclaiming in the political arena, which is also a concern for stem cell research.⁵⁷ It keeps everyone honest.

In addition to advancing science, public sponsors also have an interest in preserving intellectual property rights in research results. The Bayh-Dole Act articulates a federal government interest in ensuring that research discoveries made in the course of funded research are effectively disseminated and utilized.⁵⁸ Although one might expect the interests of state sponsors to be similar to those of the federal government, CIRM in fact faces more significant (and more parochial) constraints under the terms of Proposition 71. In

⁵⁶ See Sei Choing & Dennis Normile, *How Young Korean Researchers Helped Unearth a Scandal . . . And How the Problems Eluded Peer Reviewers and Editors*, 311 SCIENCE 22-25 (Jan. 6 2006)

⁵⁷ See David A. Shaywitz, *Stem Cell Hype and Hope*, Washington Post (Jan. 12, 2006) at A21, posted at <<http://www.washingtonpost.com/wp-dyn/content/article/2006/01/11/AR2006011102040.html>>

⁵⁸ 35 U.S.C. § 200. Other interests noted in the Bayh-Dole statute include encouraging participation of small business firms in federally supported R&D, promoting collaboration between commercial concerns and nonprofit organizations, promoting competition and enterprise without unduly encumbering future R&D, promoting "the commercialization and public availability of inventions made in the United States by United States industry and labor," ensuring that the Government obtains sufficient rights in federally supported inventions to meet its needs, and minimizing administrative costs. *Id.* Federal research sponsors are not charged by statute with recovering revenues from technologies patented by grantees except in the case of inventions made in a Government-owned-contractor operated facility (i.e., a national laboratory). Under 35 U.S.C. § 202(c)(7), sponsors are directed to include in funding agreements requirements for sharing royalties with inventors and for using remaining income, after payment of costs, to support scientific research or education. A different rule applied to funding agreements for the operation of a Government-owned-contractor-operated facility; these agreements are to require payment to the U.S. Treasury of 75% of the excess revenues after payment of expenses if the balance exceeds 5 percent of the annual budget of the facility. 35 U.S.C. § 202(c)(7)(E). Although the Bayh-Dole Act directs grantees to give a preference in the award of exclusive licenses to firms that agree to manufacture the invention in the United States, if that constraint proves to be problematic, the sponsor may waive it. 35 U.S.C. § 204.

addition to promoting the development of stem cell therapies, Proposition 71 identifies a number of goals that are more narrowly focused on the interests of California constituencies, including to “[p]rotect and benefit the California budget ... by providing an opportunity for the state to benefit from royalties, patents, and licensing fees that result from the research;” to “[b]enefit the California economy by creating projects, jobs, and therapies that will generate millions of dollars in new tax revenues in our state;” and to “[a]dvance the biotech industry in California to world leadership, as an economic engine for California’s future.”⁵⁹ Proposition 71 enhances the likelihood that the California focus of these goals will be taken to heart in its requirements for the composition of the ICOC, the committee charged with governing CIRM, which specify California institutional affiliations for each member.⁶⁰

Of course, it is not at all surprising that a California voter initiative for the appropriation of \$3 billion in research funding would be designed to promote the interests of California constituencies. Indeed, even the federal government made a similar move to promote the interests of U.S. firms in the Bayh-Dole Act by directing recipients of US research funding to give preferences for exclusive licenses to firms that would manufacture in the U.S.⁶¹ Preferences for local interests provide strategies for allowing taxpayers to capture the benefits of programs that they are paying for. To the extent that spillovers limit the incentives of governments to invest in R&D, such strategies may be necessary to motivate these investments. But local preferences in the management of IP are more troubling than national preferences because they are more limiting. If state-sponsored R&D initiatives were to become more prevalent, a proliferation of local preferences might threaten to balkanize valuable intellectual property in the hands of different owners in different states, making it difficult for firms to collect the rights they need to move forward with product development. Even a single state-sponsored research initiative such as CIRM could impose significant restrictions on dissemination through the use of local preferences if it controls access to broad, cross-cutting technologies like stem cells that may have implications for a range of problems. Such technologies are likely to have their greatest value if they are broadly disseminated to scientists and firms without regard to geography or political constituencies.

Although the authors of the Bayh-Dole Act and of Proposition 71 focused on intellectual property rights in technologies emerging from sponsored research, dissemination of data emerging from sponsored research poses similar tradeoffs between capturing value for political constituencies and promoting scientific progress. The challenge for CIRM is to figure out how to capture an adequate return on its investment in stem cell research for its constituents without unduly limiting its overall social value. In what follows, we consider this overall challenge in light of specific issues that any effort to promote data sharing must consider.⁶² These issues divide roughly into four highly interdependent categories: 1) incentives to contribute data; 2) access (who gets

⁵⁹ Proposition 71, *supra* note, Sec. 3.

⁶⁰ Proposition 71, *supra* note, Sec. 5, proposed Chapter 3, Art. 1, *California Stem Cell Research and Cures Act*, § 12590.20(a).

⁶¹ Note, however, that if that constraint proves to be problematic, the sponsor may waive it. 35 U.S.C. § 204.

⁶² For purposes of this paper, we put to one side knotty problems regarding privacy that might be raised by data associated with personally identifiable information. We assume for purposes of the paper that the data involved in stem cell research would not trigger concerns about personally identifiable information, or that the data could be effectively anonymized to address such concerns.

access and under what conditions); 3) what gets deposited and when; and 4) database architecture, maintenance, and curation. Throughout our discussion, we draw upon the experience of prior database initiatives, particularly at the federal level, that have attempted to promote widespread dissemination and sharing. In the absence of information on specific research that is likely to be funded, we make these observations at a relatively high level of generality.

Incentives to Contribute

In order to work, data release policies must provide scientists clear incentives to contribute their data. Incentives are necessary because most rewards in research science, including academic appointments, promotion, and grant funding, depend on a record of frequent publication. Scientists may perceive sharing data, even after an initial publication, as providing advantages to competitors in the race to generate further publications. Emerging evidence reveals that some research communities in the life sciences are reluctant to share data after publication. For example, a survey conducted by Eric Campbell and his colleagues found that 47% of academic geneticists had been denied access to data or materials associated with a published article at least once in the preceding 3 years.⁶³ The Campbell study did not distinguish between data and tangible materials. Because one important impediment to sharing identified by the study – the effort and financial cost associated with replication and transfer⁶⁴ – is much lower for data than for tangible materials, the study may overestimate impediments to data disclosure. Nonetheless, as discussed earlier, a series of workshops and reports emanating from the biomedical research community confirms a growing perception of departures from the principle of data sharing upon publication.⁶⁵ Anecdotal evidence indicates that some life science researchers condition data transfer on co-authorship of any subsequent publications.⁶⁶

Although NIH now requires grant applicants to include a data sharing plan in grant applications exceeding \$500,000 per year,⁶⁷ so far it has done little to follow up on compliance. If CIRM wants its grantees to share data, it should consider mechanisms for ensuring compliance with the plan from the outset in order to offset the powerful incentives that scientists face to withhold access to data. Possible mechanisms might include not only sanctions for noncompliance (such as loss of continued funding) but also rewards. One possible reward might involve privileged access to particular data analysis tools for those who contribute data to an archive. CIRM could also track downloads of

⁶³ Eric Campbell et al., *Data Withholding in Academic Genetics: Evidence from a National Survey*, 287 JAMA 473 (2002).

⁶⁴ *Id.* at 478.

⁶⁵ See, e.g., National Research Council, *Sharing Publication-Related Data and Materials: Responsibilities of Authorship in the Life Sciences* (Nat'l Acad. Press 2003). See generally National Research Council, *Bits of Power: Issues in Global Access to Scientific Data* (1997). Similarly, John Walsh and Wei Hong report that in a survey that they conducted of experimental biologists in 1998, only 14% were willing to talk openly about their current research. John Walsh and Wei Hong, *Secrecy is Increasing in Step With Competition*, 422 NATURE 801 (2003).

⁶⁶ Cite to WSJ article

⁶⁷ See *supra* ____.

data from a centralized archive and give special acknowledgements or other rewards to depositors whose data was downloaded frequently.⁶⁸

It may be easier to achieve compliance within a tightly knit community of scientists that interact frequently. For example, at the height of the Human Genome Project (HGP) the five major production labs that contributed large amounts of sequence to the public GenBank database were all talking via teleconference on a weekly basis.⁶⁹ In this environment the normative pressure to comply with data disclosure – even pre-publication disclosure – was unusually strong. Some users of data from the HGP and other community resource projects have also argued that widespread data availability was the *quid pro quo* for the major centers receiving large sums of money to complete these projects without undergoing peer review of each individual portion.⁷⁰ CIRM may be able to create similar normative pressure to comply with data disclosure obligations if it funds large-scale, centralized data production (for example, funding several large centers to produce data on gene expression at different stages of stem cell differentiation).

It bears emphasis, however, that the HGP was motivated not only by a public-spirited desire to make data quickly available (without any background patents on associated material)⁷¹ but also by a competitive desire to outdo rival private sector efforts. Measures of the volume of data accumulating in GenBank served as a conspicuous marker of accelerating productivity for the HGP. Public availability served as a salient point of distinction from the proprietary databases of commercial rivals, helping to justify continued public support for a project that appeared to substantially duplicate work that was being done in the private sector. Rapid data availability not only created prior art that might defeat future gene sequence patents,⁷² it also undermined the viability of private sector business models that entailed charging license fees for database access. Although they were able to raise investment capital to create their databases, private

⁶⁸ Although rewards of this sort might not be as attractive as preserving exclusive access so as to mine the data for additional publications (particularly if university tenure and promotion committees continued their current practice of considering publication to be the primary benchmark of success), they might provide some incentive.

⁶⁹ Interview with Tim Hubbard

⁷⁰ Steven Salzberg, Ewan Birney, Sean Eddy, Owen White, *Unrestricted Free Access Works and Must Continue*, 422 NATURE 801 (2003) (correspondence from bioinformaticians arguing that obligations of scientists in large scale data production centers differ from those of traditional scientists).

⁷¹ In February 1996, scientists from the major sequencing centers in the HGP explicitly disavowed patenting. Eliot Marshall, *Genome Researchers Take the Pledge: Data Sharing*, SCIENCE, April 26, 1996, at 477. NIH followed up with an April 1997 policy statement strongly discouraging patenting by HGP grantees. NHGRI Policy Regarding Intellectual Property of Human Genomic Sequence, April 9, 1997. Though it may be in some tension with Bayh-Dole, see Arti K. Rai and Rebecca S. Eisenberg, *Bayh-Dole Reform and the Progress of Biomedicine*, LAW AND CONTEMPORARY PROBLEMS (2003), this “no patenting norm” has also been part of subsequent NIH-sponsored “community resource” projects.

⁷² Although raw genomic data would not undermine claims to specific genes of identified function, annotated data might do so. A major goal of annotation is to identify coding regions in the genome and add information about the function of the protein for which the region codes. A recent empirical study suggests that at least 20% of human genes are in fact covered by patents (and some genes are covered by multiple patents). See Fiona Murray and Kyle Jensen, Science article. The extent to which these patents are valid over the prior art is unclear.

sector rivals were ultimately not able to survive in the database business.⁷³ Given its mandate to “advance the biotech industry in California to world leadership, as an economic engine for California’s future,”⁷⁴ it seems unlikely that CIRM will want to drive out private sector data producers in any large-scale data production efforts that it might fund.

Recent community resource projects in genomics have sought in a variety of ways to preserve some of the rewards of publication for scientists who contribute to public databases prior to publication. A report from the Wellcome Trust on *Sharing Data from Large-scale Biological Research Projects: A System of Tripartite Responsibility* proposes that producers of database resources publish a project description at the beginning of the project that will describe the plans of the data producers for production, analysis and release of the data and provide a citation for referencing the sources of the data.⁷⁵ It also admonishes data users to cite the source of data and to “recognize that the resource producers have a legitimate interest in publishing prominent peer-reviewed reports describing and analyzing the resource that they have produced (and that neither the Project Descriptions nor data deposits in databases are the equivalent of such publications).” The report also urges users to “act responsibly to promote the highest standards of respect for the scientific contributions of others,” which “might best be done by discussion or coordination with the resource producers.”⁷⁶ In comparable community resource projects, CIRM could use its leverage with both data producers and data users that it funds to get them to follow these suggested principles.

It is important to be mindful, however, of the inherent tension between preserving opportunities for data producers to publish their own future analyses of the data that they have disclosed and allowing other users to make free use of the data. Specific community resource projects have implemented these norms in ways that restrict publications. One of these projects, the Genetic Association Information Network (GAIN), a public-private partnership of the National Institutes of Health and several private firms (currently Pfizer, Affymetrix, and Abbott Laboratories) aims to understand the complex set of genetic factors influencing risk for common diseases by conducting a series of whole genome association studies that employ samples from patients with such diseases. The GAIN publication policy gives contributing investigators a period of nine months in which they have the exclusive right to submit publications based on their data,

⁷³ The major private sector rival to the public database, the Celera group led by Craig Venter, was ultimately unsuccessful in its efforts to charge for its database and released its data into the public domain. Emma Marris, *Free Genome Databases Finally Defeat Celera*, 435 NATURE 6 (2005). Although public availability of the human genome avoids the potentially crippling costs that might have been associated with negotiating access, and is thus a welcome development, the presence of a private sector rival had some benefit. The private sector effort arguably provided the competition necessary for the public sector to work efficiently. In particular, private sector competition may have been the catalyst necessary to overcome the public sector’s resistance to the whole genome shotgun sequencing approach, a methodology that has proved to be successful. See Eisenberg & Nelson, *A Fruitful Tension*, *supra* note .

⁷⁴ Proposition 71, Sec. 3.

⁷⁵ See *supra* note .

⁷⁶ *Id.* at 4.

while giving approved users (who sign a restrictive agreement) access to the data during this period.⁷⁷

The model adopted for community resource projects in genomics is likely to be inappropriate for decentralized, investigator-initiated work. For such work, the federally funded Protein Data Bank (PDB) may be a more apt model. In 1971, a group of crystallographers established the PDB as a centralized repository for three-dimensional protein structure data. But deposition of structures did not begin in earnest until the 1980s, as the community began to see collective advantages to deposition. In 1989, the International Union of Crystallography reinforced community views by calling on researchers to deposit data once a research article based on the data was submitted for publication.⁷⁸ Actual data release did not have to be immediate, however: researchers were allowed to request a one-year hold before public release of the data by the database.⁷⁹ This one-year hold was justified as a reward for the difficulties associated with determining protein structure.

As the difficulties associated with determining such structure decreased, leaders within the community began to call for immediate release of data upon publication. In 1999, NIH announced a policy of data release upon publication for its grantees.⁸⁰ Major scientific journals such as *Science* and *Nature* now require data deposition in PDB as a condition of publication.⁸¹ The PDB story illustrates that protein crystallographic community's scientific leaders have worked with sponsors over several decades to make data deposition an essential aspect of publication.⁸² Sustained efforts by these scientists, combined with sponsor pressure, have made the PDB central to work in the field. The experience of the PDB suggests that, in order for data sharing in routine CIRM-funded work to be successful, some combination of sustained sponsor pressure and leadership from key leaders in the stem cell community will be critical.

Finally, it bears emphasis that, in contrast with recent community resource projects in genomics, the PDB effort does not have a prohibition on patenting. Although the PDB does not keep track of background patents,⁸³ protein structure data could be associated with background patents on the gene, protein crystal, or perhaps even on a computer model of a protein binding pocket that purports to allow the investigator to test drug candidates *in silico*.⁸⁴ In a decentralized project such as PDB, a prohibition on patents might have served as a significant disincentive to scientific participation.

⁷⁷ GAIN Data Access Policy (updated as of April 26, 2006) at 3; GAIN Data Use Certification Terms of Access ¶ 6.

⁷⁸ NRC Report, Sharing Publication-Related Data, at 74-75.

⁷⁹ *Id.* at 75.

⁸⁰ *Id.* at 76.

⁸¹ *Id.*

⁸² Interview with Helen Berman, March 2, 2005.

⁸³ *Id.*

⁸⁴ Although the last category of patent appears quite close to a patent on data, the PTO has issued such patents.

Incentives to contribute are also likely to be affected by scientists' perceptions regarding who is getting access to their contributions, and under what conditions. More generally, the issue of access is an important one, both for ensuring maximum benefit from CIRM-sponsored research and for determining how CIRM, and the state of California more generally, reaps return on its investment. We turn next to questions of access.

Access: To Whom, and Under What Conditions

A pure public domain approach to scientific resources would place no restrictions on who could seek access or on what they could seek. In the area of publication-related biomedical materials, CIRM has already departed from a pure public domain approach. Instead, it has enunciated a policy that favors California researchers. The CIRM IPPNO requires grantees to share biomedical materials described in published scientific articles within 60 days of receiving a request for such materials. But grantee obligations appear to be limited to those who are seeking the materials for "research purposes in California."⁸⁵ CIRM has also directed that some of the revenue grantees receive from patent licensing be returned to the state of California.⁸⁶

In the context of data, researchers with access to CIRM-funded databases might encompass: a) CIRM-funded nonprofit researchers only; b) all CIRM-funded researchers; c) all California researchers; d) all stem cell researchers who had contributed their own data (and/or agreed to contribute their own annotations/improvements into the database); or e) all stem cell researchers. Certain categories of researchers could be excluded altogether, or they could be given access under restrictive conditions. For example, for-profit institutions (or non-California institutions) might be required to pay for access. Non-price tiering of access might include early access by certain favored categories of researchers.

Providing preferential access to CIRM-funded researchers, or to researchers based in California, could promote Prop 71's goal to stimulate the California economy. Charging for-profit institutions for access may promote the goal of direct returns to the California budget. And giving preference to those who themselves contribute data (whether through initial contributions or through improvement/annotations to the initial contribution) could provide an additional incentive to contribute. These benefits come at some cost, however: the more conditions CIRM places on access, the more potential investigators are excluded. Moreover, because data are not protected by intellectual property rights, contract-based access must specifically include restrictions against the possibility of dissemination to third parties not covered by the contract. Thus in order for any contractual restrictions to be effective, they must include a restriction on further dissemination.

⁸⁵ CIRM IPPNPO at 16. Similarly, the IPPNPO restricts its requirement that CIRM-funded patents materials be made available for research purposes to "California research institutions." *Id.* at 18.

⁸⁶ *Id.* at ____.

Again, recent experience with publicly funded databases in genomics provides a useful lens through which to analyze the difficult tradeoffs presented. In the case of the HGP, the data was put into the public domain for everyone to use without restriction. The public domain approach was chosen over the objection of some public sector scientists, who were concerned that merely creating prior art was not the most aggressive weapon for defeating proprietary claims. Because the data were freely available in the public domain, those who accessed the data were free to mix it with their own privately held information and to make the combination proprietary.⁸⁷ These scientists became particularly concerned when Craig Venter, the major private sector challenger to the HGP, appeared to adopt this approach.⁸⁸

The frustration of these public sector scientists appears to have influenced the approach towards subsequent community resource projects. The International Haplotype Map (HapMap) project, which receives funding from both the NIH and the Wellcome Trust, took a very different approach to initial data release. In that case, the raw data on single base DNA variations, also known as single nucleotide polymorphisms or SNPs, was not put into the public domain. Rather, it was made available via a clickwrap license explicitly modeled on the General Public License used by open source software developers (GPL).⁸⁹ Until December 2004, when the license restrictions were lifted, this license prohibited licensees from taking the data and combining it with their own data so as to seek product patents on combinations of SNPs known as haplotypes.⁹⁰ By the time the restrictions were lifted, HapMap leaders believed that they created enough SNP density to have prior art against most of the product patents about which NIH was most worried.

The HapMap illustrates some of the difficulties involved in adapting the GPL to the release of biomedical research data. First, the GPL is structured as a license to intellectual property rights. In the context of open source software, the licensed rights consist of copyright in software, a right that has been recognized by Congress and the courts. Under U.S. law, there is no comparable intellectual property right in data to anchor the HapMap license. The HapMap license denies this difficulty, requiring those who would access the data to acknowledge, contrary to legal authority, that the data are protected by U.S. copyright law.⁹¹ This is a problematic requirement that is paradoxical

⁸⁷ JOHN SULSTON AND GEORGINA FERRY, *THE COMMON THREAD: A STORY OF SCIENCE, POLITICS, ETHICS, AND THE HUMAN GENOME* __ (2002)

⁸⁸ There is some controversy over the extent to which the Venter project actually relied on the public data.

Cite to exchange of letters in PNAS

⁸⁹ [cites]. The International HapMap Project Public Access License Version 1.1(Aug. 2003) includes an acknowledgement to the GNU General Public License of the Free Software Foundation.
<<http://www.hapmap.org/cgi-perl/registration>>

⁹⁰ See International HapMap Project Public Access License ¶2.b.i. (“you shall not file any patent applications that contain claims to any composition of matter of any single nucleotide polymorphism (“SNP”), genotype or haplotype data obtained from the Genotype Database or any SNP, haplotype or haplotype block based on data obtained from the Genotype Database.” available at <http://www.hapmap.org/cgi-perl/registration>> Haplotypes are SNP clusters that are inherited together. Haplotypes associated with particular phenotypes can be used as markers for diagnostic tests and drug targets.

⁹¹ See *id.*, Terms and Conditions for Access to and Use of the Genotype Database, ¶ 5:

in the context of an agreement that purportedly aims to keep data freely available. Second, because there is no property right that survives disclosure to those not bound by the license, in order to ensure that third parties do not gain access to the data without agreeing to the terms of the license, the HapMap license imposes strict restrictions on dissemination. Researchers who accessed the data prior to December 2004 could not release the data to anyone who was not bound by the same license terms. Most notably, they could not include the data in publications based on the data.⁹² Third, the GPL is designed to preclude all downstream restrictions on dissemination, an approach that is possible in the area of software, where intellectual property has never been a particularly strong driver of R&D. In contrast, in the biopharmaceutical area, patents – particularly downstream patents on therapeutics – are clearly important. The HapMap license seeks to avoid imperiling downstream patents that might matter for future development through the use of complex and ambiguous license provisions that appear to prohibit product patents on SNPs or haplotypes⁹³ but may allow for process patents on various uses of SNPs and haplotypes.⁹⁴ Finally, the enforceability of open source licenses remains a somewhat open question. Clickwrap licenses are generally considered enforceable contracts.⁹⁵ However, if a public funding agency were to bring a breach of contract action against a license violator, the measure of damages would be unclear. Perhaps alleged infringers of patents that were obtained or enforced in violation of the agreement could assert that the patents were invalid or unenforceable for inequitable conduct, but there is no clear authority for such an expansion of the boundaries of inequitable conduct doctrine. Perhaps such agreements are better understood as efforts to define norms of forbearance from enforcement of intellectual property rights within a scientific community than as binding agreements that are themselves enforceable in a court of law.

“You acknowledge that the Genotype Database and the data contained in it, to which access is provided under the terms of this License, are protected by law including, but not limited to, copyright laws of the United States”

⁹² *Id.*, Paragraph G ([W]hile you are free to publish the results of those analyses [of genotypic information], you may not include in such publications the details of the individual genotypes that the Project has not yet released.”)

⁹³ International HapMap Project Public Access License ¶2.b.i. (“you shall not file any patent applications that contain claims to any composition of matter of any single nucleotide polymorphism (“SNP”), genotype or haplotype data obtained from the Genotype Database or any SNP, haplotype or haplotype block based on data obtained from the Genotype Database.”). The policy explaining the license is more ambiguous on the question of product patents. It suggests that patents (presumably both product and process patents) on haplotypes with identified utility are acceptable so long as they don’t block access to the underlying HapMap Data. *See* Data Access Policy for the International HapMap Project ¶ E (“This licensing approach is not intended to block the ability of users to file for intellectual property protection on specific haplotypes for which they have identified associated phenotypes, such as disease susceptibility, drug responsiveness, or other biological utility, as long as public access to and use of, the data produced by the HapMap Project is preserved.”)

⁹⁴ *Id.* at ¶ 2.b.ii. (“you shall not file any patent applications that contain claims to particular uses of any SNP, genotype or haplotype data obtained from the Genotype Database or any SNP, haplotype or haplotype block based on data obtained from, the Genotype Database, unless such claims do not restrict, or are licensed on such terms that they do not restrict, the ability of others to use at no cost the Genotype Database or the data that it contains for other purposes.”)

⁹⁵ *cite*

More recent community resource projects have been less aggressive in their approach to restricting future intellectual property claims. Like the HapMap license, the GAIN Data Use Certification requires those who access the data to refrain from disclosing the data to anyone who is not bound by the same agreement.⁹⁶ It also urges registrants not to rely on GAIN-supported data to seek patents on markers that might be useful in diagnosis or identification of drug targets.⁹⁷ However, the language is entirely hortatory, calling upon approved users to “acknowledge the intent” of the GAIN IP policy, reminding them that “[i]n this spirit, it is expected “that data and conclusions will remain freely available, and stating that GAIN “encourages” compliance with various NIH policies that favor sharing.⁹⁸ Further, the document explicitly “recognizes the importance of the later development of IP on downstream discoveries, especially in therapeutics . . .”⁹⁹ The less rigid language used in the GAIN Data Use Certification makes good sense given the difficulty of determining *ex ante* just what patents will prove necessary to preserve incentives for product development in the biopharmaceutical area.¹⁰⁰

What Gets Deposited and When

A third set of questions concerns what data get deposited and when. One benchmark is the standard set in the National Research Council report *Sharing Publication-Related Data and Materials*, which refers to publications to determine the scope of disclosure obligations and calls for disclosure of “the data, algorithms, or other information that is central or integral to the publication – that is, whatever is necessary to support the major claims of the paper and would enable one skilled in the art to verify or replicate the claims.”¹⁰¹ But just what this means is likely to change in any given scientific community over time. In the case of the HGP, for example, the community originally determined that sequence assemblies of 1-2 kilobases or greater should be released. However, when the community switched in part to a different sequencing methodology (the whole genome shotgun approach), which did not assemble completed sequence until much later in the project, it determined that tying data release to assembly was no longer appropriate. In 2000, NIH extended its release policy to include submission of raw sequence traces. Similarly, in the case of the Protein Data Bank, requirements for what gets deposited have evolved. Initially, only atomic coordinates were deposited. However, scientists subsequently determined that atomic coordinates did not necessarily provide all the information necessary for verification and improvement. So now there is general agreement that structural factors, the raw information from which coordinates are derived – should be deposited.¹⁰²

⁹⁶ GAIN Data Use Certification ¶4.

⁹⁷ *Id.* ¶ 5.

⁹⁸ *Id.*

⁹⁹ *Id.*

¹⁰⁰ Alternatively, it may reflect a recognition that simple release of GAIN-supported data is all that is necessary to invalidate marker patents.

¹⁰¹ SHARING PUBLICATION-RELATED DATA AND MATERIALS AT 5

¹⁰² Interview with Helen Berman

The issue of when data should be deposited is a critical one. As already noted, for community resource projects in genomics the public sponsors have generally required immediate, *pre-publication* deposit.¹⁰³ CIRM should recognize, however, that pre-publication release of data is highly unusual in science. The data release policies for community resource projects in genomics offer a precedent for centralized data production projects that CIRM might fund, but it is unlikely that scientists could be persuaded to agree to pre-publication release beyond that context. Pre-publication data release might not even be desirable for ordinary investigator-driven science, because it would interfere with the incentives provided by the reputational benefits that attach to publication.

On the other hand, a significant drawback to the current system of tying data release to publication is that negative data often remain undisclosed. CIRM might be able to address this bias in a data release policy by requiring disclosure not only of the data that leads to the publication but also of any negative data that emerged along the way. Indeed, because negative data can be so useful for future researchers, CIRM could perform a valuable service by establishing data archives that require deposits of both positive and negative data.

Finally, the distinction between pre-publication data deposit and data deposit upon publication rests on a model that currently prevails in the life sciences in which peer review precedes print publication. This distinction may become less important in the future if the life sciences community adopts a model similar to that used in the physics community, as well as in other scholarly communities, where Web-based publication precedes peer review.

Database Architecture, Curation, and Maintenance

A last set of issues relates to database architecture, curation, and maintenance. A centralized, Web-based data archive is the most obvious platform for data sharing. In biomedical research, some of the most prominent databases – GenBank for DNA sequence data and the PDB for 3-D structure data – are centralized repositories. A major advantage of a centralized database is that data are prominently available in a uniform, readily searchable format. Disadvantages include cost and the need for agreement on data standards. Even with these disadvantages, a centralized database is probably most appropriate for critical data that is most useful when aggregated, such as data on gene expression or on the characteristics of available stem cell lines. Another type of format that might be useful for certain types of projects is a federated approach, in which data are maintained and controlled at the local level but can be integrated across databases. Federated systems might be useful even in situations where the core data reside on a central server. For example, the distributed annotation system (DAS) that can be used on genomic data deposited at EMBL, the European counterpart to Genbank, allows those who want to annotate genomic data to do so on their own servers. Other DAS users can then designate which server annotations they want to layer over the core data.¹⁰⁴ The format that is probably least useful, but may nonetheless be sufficient for certain projects, is posting on a local lab server.

For all three types of databases – centralized, federated, and local – funding for ongoing curation and maintenance is critical. Indeed, one of the central problems facing

¹⁰³ Reaffirmation and Extension of NHGRI Rapid Data Release Policies: Large-Scale Sequencing and Other Community Resource Projects, February 2003, available at <http://www.genome.gov/10506537> See also *supra* ____

¹⁰⁴ Interview with Lincoln Stein; see also Lincoln D. Stein, Sean Eddy, and Robin Dowsll, Distributed Annotated System, available at <http://biodas.org/documents/rationale.html>

life sciences databases today is that funds for curation and maintenance are often not available. A recent survey of 89 life science databases determined that 51 are struggling financially: they have either been shut down for lack of funding or are being updated sporadically.¹⁰⁵ As it considers what types of research to fund, CIRM should be aware of the importance of providing funding for the ongoing curation and maintenance of databases that are important resources for the stem cell community.

¹⁰⁵ *Databases In Peril*, 435 NATURE 1010 (2005).

APPENDIX D:

THE USE OF MTAs TO CONTROL COMMERCIALIZATION OF STEM CELL DIAGNOSTICS AND THERAPEUTICS

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I. INTRODUCTION: MATERIAL TRANSFER AGREEMENTS

The recent focus on patents as a hindrance to research generally, and stem cell research in particular, may turn out to be a red herring. The real culprit seems to be material transfer agreements (MTAs) that govern the transfer of physical property such as cell lines.¹⁰⁶ The MTA's primary purpose in life sciences research is to set contractual rights and obligations between parties where one is transferring actual biological materials to the other.¹⁰⁷ For example, MTAs may "require the recipient to exercise care in the handling of the materials, to maintain control over the distribution of the materials, to acknowledge the provider in publications, and to follow relevant [Public Health Service] guidelines relating to recombinant DNA, protection of human subjects in research, and the use of animals."¹⁰⁸ These interests are all quite legitimate, however as discussed further below, there is evidence that owners of important biological research materials are using their non-patent property rights to require recipient consent to arguably onerous MTAs. When the intended recipient's institution refuses to sign the MTA, the researcher is effectively blocked from accessing the biological materials, and in some cases then blocked from pursuing her research.

Confusion surrounds MTAs because they can also include intellectual property (IP) licenses.¹⁰⁹ However, the physical property rights conveyed by an MTA must always be analyzed as distinct from whatever IP rights might also be conveyed by the MTA. In some MTAs, the transferor makes explicitly clear that the recipient may need IP licenses from third parties to use the biological materials transferred for the recipient's

¹⁰⁶ See John P. Walsh, Charlene Cho, Wesley M. Cohen, *Roadblocks to Accessing Biomedical Research Tools* (presentation at CSIC/OECD/OEPM Conference, "Research Use of Patented Inventions" Madrid, Spain, 18-19 May 2006) available at <http://www.oecd.org/dataoecd/40/12/36816897.pdf>.

¹⁰⁷ See Department of Health and Human Services, Uniform Biological Material Transfer Agreement: Discussion of Public Comments Received; Publication of the Final Format of the Agreement, __ F.R. __ (March 8, 1995).

¹⁰⁸ *Id.*

¹⁰⁹ See Memorandum of Understanding between WiCell Research Institute, Inc. and Public Health Service, art. 1 (September 5, 2001).

specific research purposes.¹¹⁰ However, one would assume that the transferor is conveying at least an implied IP license that the delivery of the biological materials from the transferor to the recipient has not violated any IP rights.

One fascinating, and perhaps poorly understood, aspect of MTAs in the life sciences is that generally they do not convey ownership of the actual biological materials transferred, but rather only a type of lease or rental of the materials.¹¹¹ I refrain from using the term “license” here because it may only add to the confusion with any IP licenses that are included in the MTA. However, my sense is that most institutions refer to the legal conveyances of permission to use the biological materials *qua* physical property as well as *qua* IP as “licenses.” This dual “lease-license” model is hardly unique to life sciences MTAs, of course – it is also the underlying model for much of the software industry, the original Bell telephone service, commercial test prep materials, musical scores made available for school performances, many of the original cable television services, and even the controversial recent practice of “bag tags” in the seed and agricultural biotechnology industries. An interesting twist is that in some of these examples, as well as in most life sciences MTAs, the physical materials are often not expected to be returned at any time to the transferor. The recipient may destroy them or retain them indefinitely; the restriction is on further transfers by the recipient. For example, few software vendors require that purchasers (really licensees, or at least purchasers of lease-licenses) return the CD-ROMs that software is delivered on. Test prep services sometimes require a refundable deposit on materials that is then returned when the materials are returned to the company. But if the consumer fails to return the materials he simply forfeits the deposit (while remaining bound by the transfer restrictions of course). Seeds transferred under bag tag licenses are perhaps the ultimate example of this practice in that they are, of course, destroyed through the very use for which they were leased-licensed to the farmer.¹¹²

So, if the transferor is not expecting to recollect the materials, then why lease them out – rather than sell them – in the first place? Presumably, one could charge a higher upfront payment for an outright sale than a lease. Other common lease situations such as auto leases or real estate rentals are likely premised on potentially greater economic returns over time through the continued payments by the lessee/tenant. But in most of the lease-license models given above, including biological materials MTAs, there are rarely ongoing payments required.¹¹³ Instead, transferors who use lease-license models may well be seeking other important legal and business advantages that might be forfeited in a sale model. These advantages generally fall into two categories: control of

¹¹⁰ See American Type Culture Collection, Material Transfer Agreement (last updated September 8, 2003) available at <http://www.atcc.org/documents/mta/mta.cfm>.

¹¹¹ See Memorandum of Understanding between WiCell Research Institute, Inc. and Public Health Service, art. 2 (September 5, 2001); American Type Culture Collection, Material Transfer Agreement (last updated September 8, 2003) available at <http://www.atcc.org/documents/mta/mta.cfm>.

¹¹² This, however, does lead directly to the litigated controversy in bag tag license situations whereby the farmer attempts to (re)use the next generation seeds, if any, which is generally prohibited under bag tag licenses. See, e.g., *Monsanto Company v. McFarling*, 363 F.3d 1336 (CA FC 2004).

¹¹³ Note that the original Bell telephone service and some bag tag licenses are the exceptions though in that ongoing payments are/were required for continued use or service.

IP rights/ownership; and limitations on liability to third parties. The lease-license model may also give extra business and negotiation leverage to the transferor because the recipient is usually under the risk that the transferor can both terminate the IP license and require the return of all materials – sometimes including derivative materials created by the recipient – from the recipient at the transferor’s discretion upon certain triggering events set out in the contract.

The first category – IP control – is perhaps the most important to transferors who use the lease-license model. This may also be why the IP license and the physical property lease or rental rights are often conflated in the minds of both members of the public and sometimes even the parties themselves. Essentially, the two strands of rights – IP and physical, or intangible and tangible – are often set up in the transfer agreement to mutually reinforce one another. A version of this reinforcement strategy is examined in more detail below as the focus of this article: the stem cell ownership rights exercised by the Wisconsin Alumni Research Foundation (WARF) and its affiliate WiCell Research Institute, Inc. (WiCell).¹¹⁴ But at the abstract level, this reinforcement strategy can be most easily introduced by considering it from the direction of the physical property lease reinforcing, or even enhancing, the IP license. If the physical property embodying or carrying the IP is sold outright, then arguably first sale/exhaustion doctrines¹¹⁵ can be invoked and the recipient is free to transfer the physical property or experiment on, disassemble, repair, or modify the physical property. Further, where the property is later transferred by the recipient, the original transferor/owner may now have to fear that the unknown third party recipient will use the property outside of the scope of the original IP license, including generating unlawful further copies. The original recipient could do these things as well, of course, but at least the transferor knows, to some extent, who it originally dealt with and had privity of contract with that original recipient. Importantly, the lease-license model cuts off the first sale/exhaustion doctrines for the physical property transferred and thus allows the transferor to impose a wider range of use restrictions on the recipient.¹¹⁶ Critical types of desired use restrictions (for the transferor) include prohibitions on reverse engineering – to reduce the risk of loss of trade secrets – and transfer of the physical property.¹¹⁷ Less critical, but also frequently seen, use restrictions include prohibitions on uses that might be otherwise considered to fall within fair use or research use exemptions in copyright and patent law respectively.

From the opposite direction, the IP, and licenses thereunder, reinforce claims or leverage with regard to physical property as well. This is particularly important where the biological materials could be fairly easily replicated by others without access to the

¹¹⁴ See *infra* Parts II & III.

¹¹⁵ “First sale” is generally linked with copyright, whereas “exhaustion” is usually linked with patents.

¹¹⁶ Note that there can be conditioned sales, but the use restrictions that can be enforced in that model may be more limited than those that can be enforced in the lease-license model. See, e.g., *Mallinckrodt, Inc. v. Medipart, Inc.*, 976 F.2d 700 (CA FC 1992). Another way to look at this is that the lease-license model allows the transferor to prohibit all of the user rights that might come along with first sale or exhaustion because there is no sale to trigger those doctrines. The conditioned sale model, by contrast, still triggers those doctrines.

¹¹⁷ Note that while patents and copyright still seem to dominate discussion of technology and IP transfers, trade secret protection plays a far larger role in actual practice than generally considered in the literature.

original owner's materials. Of course, the leverage in this direction was traditionally limited by the doctrines of misuse, especially patent misuse, or prohibitions on some tying arrangements under antitrust law.¹¹⁸ Under earlier interpretations of both the patent misuse doctrine and the prohibition on improper tying arrangements under antitrust law, patent owners were generally not allowed to use their patents to force others to buy the patent owner's version of non-patented staple goods. So, firms using the lease-license model were restricted in their efforts to force customers to purchase staple goods that fell outside the claims of their patents – say computer mouse pads along with patented software or hardware. However, under the recent Supreme Court decision in *Illinois Tool Works Inc. v. Independent Ink, Inc.*,¹¹⁹ the presumption of market power conferred upon a patent owner by the patent grant has been abrogated and thus actual market power must be demonstrated by an infringement defendant who wants to use patent misuse or antitrust law as a defense. Accordingly, patent owners may now be able to impose a wider range of license or use restrictions on potential licensees and purchasers. But, even under the earlier interpretations of law, they were almost certainly allowed to specify that licenses will only be given as a package deal with leases, rentals, or sales of physical embodiments of the patents that the patent owner produces. This has essentially been the strategy of the closed technologist – such as the traditional Apple Computer approach¹²⁰ – whereby the technology IP owner does not license others to bring versions of the technology to the marketplace, but rather directly manufactures, or has manufactured for its distribution, all of the permitted saleable versions of its products. Open technologists, such as IBM with regard to its PC platform,¹²¹ license out their patents for other companies to manufacture and distribute – sometimes even in some degree of competition with the pioneer technologist. While I do not recall that Apple ever used a lease-license model for its closed technology Macintosh computer platform, the original Bell telephone system very much restricted hardware choices for customers who purchased phone service. In the Bell case, affiliates such as Western Electric supplied the approved hardware to Bell customers. You could not hook up unapproved telephones or other hardware to the Bell phone lines – at least without violating your service contract. Of course, the Bell system, as part of the original AT&T, was broken up as a monopoly in violation of federal antitrust laws in 1984.¹²²

Discussion of the Bell system, however, also highlights how the sometimes underrated distinction between goods and services – as legal categories – can play a critical role in determining rights between parties. So far we have been talking about

¹¹⁸ *Illinois Tool Works Inc. v. Independent Ink, Inc.*, 126 S. Ct. 1281 (2006).

¹¹⁹ *Id.*

¹²⁰ Although Apple has recently shown signs of changing this core policy stance.

¹²¹ Recently sold off to Lenovo.

¹²² Which, of course, raises the related issue that aggressive technologists who leverage their physical and intellectual property off each other too strongly may find themselves targets of antitrust investigations by the Justice Department or Federal Trade Commission. Ultimately, of course, something close to the original AT&T has recently risen phoenix-like from the long smoldering ashes of “Ma Bell” and the “Baby Bells” when the former SBC Communications, itself a product of mergers of former Baby Bells, and the remaining long distance provider shell of the AT&T corporation merged to form the “new” at&t. Marketing and PR gurus can speculate as to the choice of lower case letters for the acronym – maybe the new at&t is supposed to be more warm and fuzzy or approachable than the perhaps imposing former “AT&T” in capital letters?

either sales of goods – covered by Article 2 of the Uniform Commercial Code (UCC) – or lease-license hybrids – covered by a combination of Article 2A of the UCC (for the lease portion) and the relevant IP law (for the licenses).¹²³ But the original Bell system seems to have been simply a *service* that provided hardware as part of the service. Still today we refer to getting “phone service,” but to the extent we think about it, we likely assume that this historically just meant the live connection transmitted by the phone line, as it is today when you can buy your own phone and peripherals. Instead, however, when one looks at old advertisements for telephone service, as well as the explanatory materials AT&T provided during the break-up to explain the difference between the phone service they had been providing and the package that customers who chose to move to other providers, or even just stay with AT&T but buy their own phones, could expect to receive, it is clear that AT&T considered itself to be providing the phones, wires, maintenance, and even phone books as part of the service. And even though AT&T’s old true phone service is gone, hardware based services are still installed in homes to this day in the form of security systems as well as some cable and satellite television services. But if the technologist is providing a service rather than either a sale of goods or a lease-license, then neither the UCC nor IP laws seem to directly apply. Instead, presumably common law rules regarding the provision of personal or professional services apply, except where specifically regulated otherwise.¹²⁴ Further, this common law realm may seem to be even more favorable to the technologist’s bid to tightly control her platform technologies. In fact, a trend in the software industry has been that of application service providers who host software applications on websites that customers can access to use the software. In this relatively recent model, the product delivered seems to be purely a service and no goods appear to be sold or leased to the customer. Thus, the technology-as-service model may yet remain with us some time longer.

Returning to the life sciences, the transfer of biological materials among researchers has probably relied on lease-license model as much because of the second category of rationales for such models – limiting potential third party liability – as for the first category just discussed.¹²⁵ As discussed in the National Institutes of Health’s (NIH) efforts to create a uniform biological MTA (the UBMTA) in the 1990s on behalf of the Public Health Service (PHS), MTAs are viewed as important because they can allow the materials owner to impose contractual obligations on the recipient “to exercise care in handling the materials, to maintain control over the distribution of the materials, . . . and to follow relevant [Public Health Service] guidelines relating to recombinant DNA,

¹²³ See NGUYEN, GOMULKIEWICZ, & CONWAY-JONES, *INTELLECTUAL PROPERTY, SOFTWARE, AND INFORMATION: LICENSING LAW AND PRACTICE* (BNA Books, *forthcoming* 2006).

¹²⁴ See *id.*

¹²⁵ Biological material transfers are probably not considered a service in most cases because the transferor does not retain control over the materials transferred to the recipient and plays no role in producing the outcome that the recipient seeks to produce in the lab. In the technology service examples discussed above, the technology owners still largely controlled and maintained the system installed in the home or business. The customer had the relatively narrow – although obviously critical in the sense of the ultimate value of the service to the customer – task of, say, dialing a phone number. Although, in the earliest days of phone service the customer did not even do that much, but rather picked up the receiver, “rang” for the operator, and requested that a call was placed by the service provider itself.

protection of human subjects in research, and the use of animals.”¹²⁶ Besides federal guidelines for the handling of biological materials – especially human materials – many states have regulations on the collection, use, and transfer of (human) biological materials.¹²⁷ Many of these federal and state guidelines center on the doctrine of informed consent.¹²⁸ Most MTAs currently in use clearly emphasize this liability limiting function.¹²⁹

But whereas other industries that have adopted lease-license models have firms providing one-to-many products, in the biological sciences research field the owners of biological materials often are not involved in such one-to-many distributions. Rather, in many cases there may only be one or a handful of distributions of the materials. Further, outside of commercial firms like the American Type Culture Center (ATCC), few if any of the non-commercial research entities that own useful biological materials, such as universities, make a business out of marketing and distributing those materials. Accordingly, where it might be cost effective for firms in one-to-many commercial distribution models such as the software industry to develop and deploy, and customers to accept, mass market licenses that may cost a lot in upfront legal fees, this kind of approach is harder to justify in the one-to-one or one-to-few world of biological MTAs.

By the early 1990s, it became clear to researchers and their institutions, including federal agencies, that MTAs were creating significant stumbling blocks in the transfer of necessary or highly important biological materials for new research.¹³⁰ The underlying issues “include delays in sharing of materials while conducting unnecessarily extensive negotiations on individual MTAs, required grants of invention rights to improvements to the materials or to inventions made using the materials, and required approval for publication.”¹³¹ The existence of these concerns in turn led to extensive “negotiation of these complex issues [which] has resulted in significant delays in sharing materials, undue administrative barriers to sharing, and in some cases, lack of availability of materials for further research by federal grantees.”¹³² NIH, in conjunction with the Association of University Technology Managers (AUTM) and representatives of universities, law firms, and industry, was ultimately able to issue a model UBMTA in 1995.¹³³ The UBMTA consists of a Master Agreement to be adopted by institutions who

¹²⁶ See Department of Health and Human Services, Uniform Biological Material Transfer Agreement: Discussion of Public Comments Received; Publication of the Final Format of the Agreement, ___ F.R. ___ (March 8, 1995).

¹²⁷ See PATRICIA KUSZLER ET AL, GENETIC TECHNOLOGIES AND THE LAW ___ (Carolina Academic Press, forthcoming 2006).

¹²⁸ *Id.* Other presentations and papers in this Symposium cover informed consent in more detail. See [cite Symposium papers/presenters].

¹²⁹ See, e.g., American Type Culture Collection, Material Transfer Agreement (last updated September 8, 2003) available at <http://www.atcc.org/documents/mta/mta.cfm>.

¹³⁰ See Department of Health and Human Services, Uniform Biological Material Transfer Agreement: Discussion of Public Comments Received; Publication of the Final Format of the Agreement, ___ F.R. 12771 (March 8, 1995) (citing 2 THE NEW BIOLOGIST 495-497 (June 1990); 248 SCIENCE 952-957 (May 25, 1990)).

¹³¹ *Id.*

¹³² *Id.*

¹³³ *Id.*

voluntarily became signatories to the UBMTA initiative, and a shorter Implementing Letter form to be used by and between signatory institutions to record specific biological material transfers.¹³⁴ However, while 286 research institutions have signed onto the UBMTA initiative to date,¹³⁵ it does not seem to have had the broad streamlining effect on biological material transfers in the research community. Part of this may be because the initiative expressly did not cover for profit organizations who might “choose to adopt this agreement as well” but were not part of PHS’ final recommendations as to target signatories/users.¹³⁶ But even in the recommended target signatory audience of public and non profit organizations, becoming a signatory to the Master UBMTA Agreement was not required by PHS, or a condition of further PHS funding.¹³⁷ Further, even among signatories, the UBMTA “would not be mandatory” so that organizations could “retain the option to handle specific material with unusual commercial or research value on a customized basis.”¹³⁸ Accordingly, the potential value of a truly uniform MTA was squandered by allowing too many exceptions. However, because of the complexity of the very same legal issues that traditionally have held up the execution of MTAs, and hence the timely transfer of biological research materials, the one-size-fits-all approach of a mandatory standard MTA may be inappropriate anyway.

II. THE CURRENT WiCELL CONTROLLED STEM CELL RESEARCH LICENSING REGIME

After reviewing the basics of life sciences MTAs in Part I, we can now examine the current WiCell controlled stem cell research environment as a case study in the power of MTAs to control life sciences research. At the same time, this case study reveals some of the important counterbalancing government rights that can be used to permit relatively unfettered research even in an environment tightly controlled by one organization. These counterbalancing rights will be briefly considered in Part III below. A central argument of this article is that these rights need to be better understood and exploited so that a proper balance can be achieved between providing appropriate economic rewards to innovators on the one hand, and reducing obstacles to next generation innovators and ensuring that some public benefits are received in exchange for public research funding, on the other.

A major breakthrough in stem cell research occurred in 1998 when Dr. James A. Thomson at the University of Wisconsin-Madison (Wisconsin) was finally able to culture immortal human embryonic stem cells (hESCs).¹³⁹ While Thomson had been able to

¹³⁴ Both documents are available at http://www.autm.net/aboutTT/aboutTT_umbta.cfm.

¹³⁵ See AUTM, Resources: Signatories to the March 8, 1995 Master UBMTA Agreement, available at http://www.autm.net/aboutTT/aboutTT_umbtaSigs.cfm.

¹³⁶ Department of Health and Human Services, Uniform Biological Material Transfer Agreement: Discussion of Public Comments Received; Publication of the Final Format of the Agreement, ___ F.R. 12771 (March 8, 1995).

¹³⁷ *Id.*

¹³⁸ *Id.* at 12771-12772.

¹³⁹ See James A. Thomson *et al* ___ 282 SCIENCE 1145-1147 (1998); *Breakthrough of the Year: Stem Cells Show Their Potential*, 286 SCIENCE ___ (December 17, 1999).

culture an immortal line of primate embryonic stem cells earlier,¹⁴⁰ the real prize was to create the human cell line. As Thomson was continuing his pioneering research in this area, WARF, as the external technology transfer office (TTO) of Wisconsin, was working to secure patent protection for the subject matter of his invention disclosures. Presumably under a version of the common university faculty policy that requires assignment of patents arising from university-based research, Thomson assigned his rights in a sequence of patents that have been issued covering stem cells to WARF.¹⁴¹

The crux of his first and second patented inventions was the ability to create stable, embryonic stem cell lines that could keep generating new embryonic stem cells indefinitely, without any of the individual stem cells beginning the differentiation process that would ultimately turn them into particularized cells for specific tissues of the adult organism, and without any of the cells undergoing significant genetic mutations. The claims of the patents are directed to both stem cells as compositions of matter and the process for creating cultures of such stem cells. As claimed in the first patent, U.S. Patent No. 5,843,780 issued in 1998 (the '780 Patent), directed to primate embryonic stem cells:

We claim:

1. A purified preparation of primate embryonic stem cells which (i) is capable of proliferation in an in vitro culture for over one year, (ii) maintains a karyotype in which all the chromosomes characteristic of the primate species are present and not noticeably altered through prolonged culture, (iii) maintains the potential to differentiate into derivatives of endoderm, mesoderm, and ectoderm tissues throughout the culture, and (iv) will not differentiate when cultured on a fibroblast feeder layer.
2. The preparation of claim 1 wherein the stem cells will spontaneously differentiate to trophoblast and produce chorionic gonadotropin when cultured to high density.
3. A purified preparation of primate embryonic stem cells wherein the cells are negative for the SSEA-1 marker, positive for the SSEA-3 marker, positive for the SSEA-4 marker, express alkaline phosphatase activity, are pluripotent, and have karyotypes which includes the presence of all of the chromosomes characteristic of the primate species and in which none of the chromosomes are noticeably altered.
4. The preparation of claim 3 wherein the cells are positive for the TRA-1-60, and TRA-1-81 markers.
5. The preparation of claim 3 wherein the cells continue to proliferate in an undifferentiated state after continuous culture for at least one year.
6. The preparation of claim 3 wherein the cells will differentiate to trophoblast when cultured beyond confluence and will produce chorionic gonadotropin.

¹⁴⁰ See U.S. Patent No. 5,843,780 (December 1, 1998).

¹⁴¹ See *id.*; U.S. Patent No. 6,200,806 (March 13, 2001); and U.S. Patent No. 7,002,252 (February 28, 2006).

7. The preparation of claim 3 wherein the cells remain euploid for more than one year of continuous culture.

8. The preparation of claim 3 wherein the cells differentiate into cells derived from mesoderm, endoderm and ectoderm germ layers when the cells are injected into a SCID mouse.

9. A method of isolating a primate embryonic stem cell line, comprising the steps of:

- (a) isolating a primate blastocyst;
- (b) isolating cells from the inner cell mass of the blastocyst of (a);
- (c) plating the inner cell mass cells on embryonic fibroblasts, wherein inner cell mass-derived cells masses are formed;
- (d) dissociating the mass into dissociated cells;
- (e) replacing the dissociated cells on embryonic feeder cells;
- (f) selecting colonies with compact morphologies and cells with high nucleus to cytoplasm ratios and prominent nucleoli; and
- (g) culturing the cells of the selected colonies.

10. A method as claimed in claim 9 further comprising maintaining the isolated cells on a fibroblast feeder layer to prevent differentiation.

11. A cell line developed by the method of step 9.¹⁴²

The upshot of the research resulting in this patent is that Thomson and Wisconsin now had a way to produce relatively large quantities of stable primate embryonic stem cells that researchers could use to conduct experiments in directing those stem cells to differentiate into specific tissues in a controlled manner. This is the holy grail of stem cell research: to essentially be able to generate any tissue of the body at will to replace diseased or destroyed tissue in specific patients. Ideally, such tissues would be created from stem cells whose genetic materials are identical to, or derived from, the patient's own genome to minimize triggering the patient's immune system into trying to destroy the new tissue as dangerous foreign cells.¹⁴³ But the first step is to master the differentiation process in any embryonic stem cells so as to be able to direct it to achieve predictable desired results. And to master the differentiation process, researchers need relatively large quantities of stable embryonic stem cells to work from. The Thomson invention claimed in the '780 Patent does essentially this, at least as broadly claimed for primates and not specifically for humans.

A lingering question is whether the '780 Patent, directed to "primate embryonic stem cells", covers hESCs as well. At one level it should, because humans are primates. But, if so, then one wonders why WARF pursued the next patent in its stem cell patents sequence, U.S. Patent No. 6,200,806 (March 13, 2001) (the '806 Patent), with essentially

¹⁴² U.S. Patent No. 5,843,780 (December 1, 1998).

¹⁴³ This patient customization step is the province of so-called therapeutic cloning research that seeks to predictably generate stable blastocysts using somatic cell nuclear transfer processes to combine a specific patient's genetic materials with a donor egg. The blastocysts can then be used to obtain embryonic stem cells containing the patient's genetic material, and thus to generate differentiated tissues/cells to replace the patient's diseased or destroyed tissues without triggering a dangerous immune response.

identical claims to the '780 Patent, but instead directed to "pluripotent human embryonic stem cells."¹⁴⁴ In fact, the '806 Patent even uses the same title – "Primate Embryonic Stem Cells" – as the '780 Patent. Further nearly all of the background descriptive material in the '806 Patent is the same as that of the '780 Patent.

While it goes beyond the focus of this article to determine what WARF's patent prosecution strategy was, two suggestions come immediately to mind. First, the "Summary of Invention" and "Description of the Invention" sections of the '780 Patent, while not determining the scope of the actual claims of that patent, indicate that a significant part of the utility of the invention was to allow researchers to "generat[e] transgenic non-human primates for models of specific human genetic diseases."¹⁴⁵ It is standard, although admittedly objectionable to animal rights activists, to use animal experiments to explore possible outcomes in humans by an analogy. Thus, WARF may have been concerned that courts would interpret the '780 Patent to cover only non-human primate embryonic stem cells. Second, WARF may have worried that the U.S. Patent and Trademark Office's (USPTO) stated policy that it will not issue patents on humans could lead courts to interpret the '780 Patent to cover only non-human primate embryonic stem cells: as just mentioned, the proposed utility of the invention in the '780 Patent seem to be that researchers could use of the patented stem cells to create actual transgenic primates with certain desirable disease traits; this could cut too close to what might be deemed a patent on humans if the scope of the claims were interpreted to cover hESCs.

The '806 Patent may remedy these potential shortcomings by changing the title of the invention description section from "Description of the Invention" to "Detailed Description of the Preferred Embodiments" and then slightly rewriting the text to make it clear that the utility of creating diseased transgenic primates is limited to the two "preferred embodiments" (best mode) of the embryonic stem cell lines described for Marmoset and Rhesus monkeys respectively. Further, the '806 Patent attempts to quell any concerns over whether the demonstrated science to date allowed claims specifically for hESC lines, even as one fitting the parameters of the claims was apparently not in existence when the application was filed, by relying on scientific arguments such as the following:

There are approximately 200 primate species in the world. The most fundamental division that divides higher primates is between Old World and New world species. The evolutionary distance between the rhesus monkey and the common marmoset is far greater than the evolutionary distance between humans and rhesus monkeys. Because it is here demonstrated that it is possible to isolate ES cell lines from a representative species of both the Old World and New World group using similar conditions, the techniques described below may be used successfully in deriving ES cell lines in other higher primates as well. Given the close distance between rhesus macaques and humans, and the fact that feeder-dependent human EC cell lines can be grown in conditions

¹⁴⁴ U.S. Patent No. 6,200,806 at col. 21.

¹⁴⁵ U.S. Patent No. 5,843,780 at col. 6

similar to those that support primate ES cell lines, the same growth conditions will allow the isolation and growth of human ES cells. In addition, human ES cell lines will be permanent cell lines that will also be distinguished from all other permanent human cell lines by their normal karyotype and the expression of the same combination of cell surface markers (alkaline phosphatase, preferably SSEA-3, SSEA-4, TRA-1-60 and TRA-1-81) that characterize other primate ES cell lines. A normal karyotype and the expression of this combination of cell surface markers will be defining properties of true human ES cell lines, regardless of the method used for their isolation and regardless of their tissue of origin.¹⁴⁶

What is curious about this approach for the '806 Patent is that Thomson formally announced that he had actually created a hESC line in a November 1998 publication in *Science*,¹⁴⁷ which presumably means that he had the line in his possession earlier than the publication date. But the application for the '806 Patent – as a division of the earlier 1995 application and continuation-in-part of the 1996 application as discussed below – was not filed until June 26, 1998. One wonders why mention of Thomson's ability to actually culture the hESC line covered in the patent does not appear; rather the patent relies on the scientific analogy argument reproduced above. There is, of course, a prohibition in patent law for introducing new subject matter into an application after the filing date that one is tracing priority back to – and WARF may well have wanted to get the 1995 or 1996 parent application dates for priority with regard to the '806 Patent – but mention of the actual hESC line would not have been introducing new subject matter. Rather, it would have been simply showing further refinement of the existing subject matter. Ultimately, an examination of the prosecution history of both the '780 Patent and the '806 Patent might yield some answers to all of these questions. However, that next step is not necessary for the focus of this article. Additionally, other practitioners and scholars are actively analyzing the WARF stem cell patents for infirmities or limitations.¹⁴⁸

Yet, even as some or all of the foregoing might explain WARF's motives in filing for the '806 Patent, it does not explain why the USPTO allowed two heavily overlapping patents to issue. Either it is an accidental incidence of double patenting – which could raise validity questions for the patents – or the USPTO believed that the claims of the '780 Patent in fact did not reach to hESCs, even as humans would normally be considered to be a species in the genus of primates.¹⁴⁹ But, if the latter interpretation is correct, there are strong ramifications for the scope of the federal government's rights and license to the WARF hESC technology. As indicated in the '780 Patent, the Thomson research leading to the invention claimed in that patent was at least partly funded by an

¹⁴⁶ U.S. Patent No. 6,200,806 at col. 6-7.

¹⁴⁷ James A. Thomson, _____ 282 *SCIENCE* 1145-1147 (1998).

¹⁴⁸ See, e.g., Kenneth S. Taymor, Christopher Thomas Scott & Henry T. Greely, *The Paths Around Stem Cell Intellectual Property*, 24 *NATURE BIOTECHNOLOGY* 411 (April 2006).

¹⁴⁹ There is precedent for valid class or genus (used as a patent law term) patent claims to not be interpreted to cover certain species (also used as a patent law term) normally considered to be within that class or genus, even as other species within the class or genus are interpreted to have been included.

NIH grant.¹⁵⁰ Thus, this means that the invention falls under the provisions of the Bayh-Dole Act of 1980 (Bayh-Dole),¹⁵¹ including the presence of a mandatory non-exclusive license granted back to the government,¹⁵² as well as the power for the government to exercise march-in rights upon certain triggering events to grant licenses under the patent to organizations not licensed by the patent owner.¹⁵³

The '806 Patent, and the most recently issued patent in WARF's stem cell patent sequence (U.S. Patent No. 7,005,252 (February 28, 2006) (the '252 Patent)), however, list either "not applicable" or simply nothing under the required "Statement Regarding Federally Funded Research" section of the patents. Accordingly, this must mean that WARF is claiming that no federal funds were used in the research leading to the patents, and hence the government licenses and rights under Bayh-Dole do not exist for these patents. In the case of the '252 Patent this claim to an absence of federal funding is entirely plausible as the patent issued directly from an application filed on March 9, 2000, and the scope of the claims and invention is clearly different from that of the '780 Patent and the '806 Patent, even as the newest patent still deals with hESC subject matter. But the '806 Patent issued as both a continuation-in-part (CIP) of the same parent application, U.S. Patent Application Serial No. 08/376,327 filed on January 20, 1995 and now abandoned (the '327 Application), that led to the '780 Patent (also as a CIP), and division of an application filed on January 18, 1996. So, even if the 1996 application introduced material outside of the scope of the '327 Application, then there is still the common subject matter arising from the '327 Application. Further, because the description of the invention, including the research relied on to justify the patentability of the inventions, is essentially the same in both patents, it seems hard to believe that the NIH grant covered research only leading to one and not the other. Unless I am missing something, I am at a loss to understand what research is not relied on in the '806 Patent but was used in the '780 Patent.

None of this hair-splitting analysis is purely academic, however, because as mentioned above, the question of whether federal funding was used to invent the subject matter covered by specific patents directly determines whether the government has the licenses and rights mandated under Bayh-Dole. To some extent, the concerns raised here are mooted because of the arrangement that PHS has worked out with WARF and WiCell, as discussed below. But, these concerns are not entirely mooted because WARF and WiCell are claimed by some to have been playing hardball even within the context of the PHS arrangement, and a failure by WARF to duly record government rights in the '806 Patent could open the patent up to challenges by either the government or infringement defendants in any suits brought by WARF to enforce the patent.

The federal funding analysis is also quite important to Geron Corporation (Geron), that began funding Thomson's research at Wisconsin and took a license from WARF to any patents that might issue under the '327 Application (the 1996 Geron

¹⁵⁰ U.S. Patent No. 5,843,780 at col. 1.

¹⁵¹ P.L. 96-517, 94 Stat 3015 (1980) (*codified at* 35 U.S.C. § 200 *et seq.*).

¹⁵² 35 U.S.C. 202(c)(4).

¹⁵³ 35 U.S.C. 203.

License).¹⁵⁴ This initial license was styled as a “Standard Nonexclusive License Agreement” by the parties,¹⁵⁵ and stated that the license granted was nonexclusive in the License section of the agreement,¹⁵⁶ but in fact Geron was also granted a renewable one-year period of exclusivity for the Licensed Patents¹⁵⁷ (defined as the ‘327 Application, any foreign equivalents, CIPs until January 1, 1998, and continuations and reexaminations¹⁵⁸). Geron was also granted an option to obtain “nonexclusive licenses” to any further inventions developed by Thomson by January 1, 1998.¹⁵⁹ But if Geron did exercise this option, then any new patents licensed under the option would be added to the definition of “Licensed Patents”, and thus presumably be subject to the period of exclusivity to the extent that Geron had continued to renew such exclusivity.¹⁶⁰ The 1996 Geron License also contemplates that federal funding may have been involved in Thomson’s research leading to the ‘327 Application, and thus carves out a limitation to the licenses, and by inference the period of exclusivity, to Geron for the potential U.S. government non-exclusive license mandated under Bayh-Dole.¹⁶¹ However, the relevant clause also proceeds to state that, “In the event there is assertion by the Government of such rights, Geron may be entitled to modification of the royalty and license fee provisions of the Agreement.”¹⁶² Thus, the answer to the question of whether federal funding was involved in the research leading to the ‘327 Application, and any follow-on applications for that matter, would have significant impact on both WARF and Geron in this license arrangement.

Despite the somewhat suspicious sounding use of a nominally nonexclusive license coupled with a “period of exclusivity” in the 1996 Geron License, I do not find anything necessarily nefarious about this agreement. There may have been good reasons for not granting an exclusive license outright – from satisfying Bayh-Dole’s own stated preference for non-exclusive licenses for federally funded patents to the parties legitimate desire to reach an agreement that possibly lowered the cost to Geron for the license (an outright exclusive license would normally fetch higher upfront license fees and royalty rates than a nonexclusive license), while giving it an option for exclusivity. To me, the latter kind of compromise arrangement, if true, is simply good, creative license negotiations.¹⁶³ Keep in mind that at the time of this original license, there was no issued patent on the science and Thomson appears to have not yet successfully cultured the hESC line. So, at that stage, WARF could only offer a license to a patent application (!) on what I often call “cool science”, meaning research results that are of significant

¹⁵⁴ See Standard Nonexclusive License Agreement between WARF and Geron (Agreement No. 95-0208) (January 1, 1996) *reprinted in redacted version* in Geron Corp. Form S-1 (filed with the Securities and Exchange Commission on June 12, 1996).

¹⁵⁵ *Id.*

¹⁵⁶ *Id.* at sec. 2(A).

¹⁵⁷ *Id.* at sec. 2(C).

¹⁵⁸ *Id.* at Appendix A, item A.

¹⁵⁹ *Id.* at sec. 2(D).

¹⁶⁰ *Id.*

¹⁶¹ *Id.* at sec. 12.

¹⁶² *Id.*

¹⁶³ Anecdotally, I have heard that technology transfer licenses – and IP licenses generally – are increasingly using options to brook disagreements in potential license terms that threaten to scuttle the deal entirely. I think this is a desirable development.

interest to the research community, and science buffs in the public, but are nowhere near a commercialized product. Note that the technology transfer license game is often just this kind of angling by outside companies to get in early enough on emerging research when leverage in the negotiation of the license may rest more with the company than with the TTO, but not too early, or too often, so that the company winds up bleeding itself dry with payments to TTOs and universities for cool science that is simply too far away from commercialization to satisfy investors. Overall, given the record available, I think both parties played their respective hands well.

One glitch, however, that seems to have cost Geron ultimately, was the bet on the January 1, 1998 date for emergent CIPs on the '327 Application as part of the definition of Licensed Patents in the 1996 Geron License. While Geron and WARF agreed to amendments of this agreement in March, 1997 and March 1998, I have been unable to track down the text of these amendments. Based on Geron's decision not to include these amendments as material contracts in its required Securities and Exchange Commission (SEC) filings, despite including the redacted text of the original license in SEC filings, one can infer that the amendments could not have been particularly important, on pain of Geron violating federal securities laws.¹⁶⁴ Assuming that nothing changed in the definition of Licensed Patents through January 1998, then the '806 Patent, and thus possibly the only claims covering hESCs, fell outside of this definition as it was filed as a CIP on the '327 Application on June 26, 1998. Tough luck for Geron, if true.¹⁶⁵ All was not lost for the company under this speculated scenario, but it would have reduced Geron's rights to the '806 Patent to simply an option to a nonexclusive license, upon timely notice and payment of a specified upfront license fee by Geron. At the same time, under my analysis of the 1996 Geron License above, if Geron had continued renewing the period of exclusivity, then because new Thomson patents for which Geron took licenses under this option right would themselves become part of the definition of Licensed Patents, Geron may have had a claim to a period of exclusivity for the '806 Patent as well.

However, I tend to think that Geron found itself without exclusivity to the '806 Patent because a new license was negotiated and executed between WARF and Geron in

¹⁶⁴ I am unaware of any publicly available sources for the licenses between Geron and WARF other than Geron's required filings with the SEC as a reporting company, as defined under the Securities Exchange Act of 1934, P.L. No. 73-291, 48 Stat. 881 (codified as amended at 15 U.S.C. §§ 78a-78hh). However, these requirements mandate only certain periodic disclosures, including agreements or contracts that are "material" to the reporting company. The 1996 Geron License must have been deemed as material to Geron, and thus was included as an exhibit to Geron's Form S-1, filed on June 12, 1996, to begin Geron's initial public offering process. But the 1997 and 1998 amendments, while mentioned in the license that supersedes the 1996 Geron License in 1999 and appears in a later SEC filing as a material agreement, appear to have not been deemed material to Geron, as they are not included in the relevant SEC filings. While amendments to a material contract would seem to me to be material themselves, I am not examining Geron's compliance with securities law in this article. Accordingly, presuming that Geron did not violate securities laws, then the contents of these amendments must not have been material.

¹⁶⁵ One could speculate as to filing date decisions by WARF, but, again I have found no evidence of underhanded activities by either WARF or Geron in any of the stem cell patents issues, despite the apparent unpopularity of WARF in this matter.

May 1999 (effective as of April 23, 1999) (the 1999 Geron License).¹⁶⁶ In the alternative, Geron could simply have desired to flip the agreement into an outright exclusive license arrangement, perhaps based upon the twin events of issuance of the '780 Patent and announcement of Thomson's creation of a viable hESC line in 1998. In any event, the 1999 Geron License is indeed a straightforward exclusive license agreement for both "Therapeutic Products"¹⁶⁷ and "Diagnostic Products"¹⁶⁸ worldwide.¹⁶⁹ The "Licensed Patents" in the agreement expressly include the '780 Patent, and, presumably, the application for the '806 Patent.¹⁷⁰ The 1999 Geron License also provides a worldwide exclusive license to the Licensed Patents for "Research Products,"¹⁷¹ essentially research tools.¹⁷² These two exclusive license grants are limited to the "Licensed Field," which includes only "(i) Research Products, (ii) Therapeutic Products and (iii) Diagnostic Products developed from and/or incorporating the Materials as precursors to [certain enumerated cell types] as well as [the same enumerated cell types]." ¹⁷³ Materials are defined as "the primate, including human, embryonic stem cells claimed in the Licensed Patents."¹⁷⁴ Finally, the 1999 Geron License also provides a worldwide nonexclusive license to the Licensed Patents for Geron to use in its internal research programs.¹⁷⁵

No doubt about it, this is a strong license for Geron. In essence, it allows the company to lock down the entire worldwide commercialization of stem cell therapies and diagnostics,¹⁷⁶ with the latter only limited to cell types enumerated in the agreement. But

¹⁶⁶ License Agreement by and between WARF and Geron Corp. (executed May 5, 1999, effective April 23, 1999) *reprinted in redacted version in* Geron Corp. Form 10-Q for period ending September 30, 1999 (filed with SEC on November 15, 1999).

¹⁶⁷ Defined as "products or services other than Diagnostic Products that (i) are used in the treatment of disease in humans, and (ii) employ, are in any way produced by the practice of, are identified or arise out of any research involving the inventions claimed in the Licensed Patents or that would otherwise constitute infringement of any claims on the Licensed Patents." *Id.* at Appendix A, item C.

¹⁶⁸ Defined as "products or services that (i) are used in the diagnosis, prognosis, screening or detection of disease in humans, and (ii) employ, are in any way produced by the practice of, are identified using or arise out of any research involving the inventions claimed in the Licensed Patents or that would otherwise constitute infringement of any claims of the Licensed Patents." *Id.* at Appendix A, item D.

¹⁶⁹ *Id.* at sec. 2(A)(i).

¹⁷⁰ *Id.* at Appendix A, item A; Appendix B (listing the '780 Patent but also including two other patent applications, titled "Primate Embryonic Stem Cells" and "Primate Embryonic Stem Cells With [...] Genes" (bracketed material in title redacted by Geron in the SEC filing) respectively, but whose application numbers and other identifying information have been redacted by Geron in the SEC filing).

¹⁷¹ Defined as "products or services that (i) are used in research as research tools which would infringe the claims of patented technology owned by Geron or which Geron has a right or license to use other than the Licensed Patents, and (ii) which employ, are in any way produced by the practice of, are identified using or arise out of any research involving the inventions claimed in the Licensed Patents or that would otherwise constitute infringement of any claims of the Licensed Patents. Research Products specifically excludes the Materials." *Id.* at Appendix A, item E. Materials are defined as "the primate, including human, embryonic stem cells claimed in the Licensed Patents." *Id.* at Appendix A, item H.

¹⁷² *Id.* at sec. 2(A)(ii).

¹⁷³ *Id.* at Appendix A, item I. The bracketed material was redacted by Geron in the SEC filing.

¹⁷⁴ *Id.* at Appendix A, item H.

¹⁷⁵ *Id.* at sec. 2(A)(iii).

¹⁷⁶ To the extent that the '780 Patent and '806 Patent continue to be interpreted as covering all current possible hESCs and their production, and that foreign patent filings by WARF are successful.

even the cell type limitation for diagnostics is not as strict as it sounds, because Geron also has a first option to negotiate exclusive licenses to new cell types that it identifies, with the further caveat that if the parties cannot negotiate the new exclusive license, then WARF may not offer a license to those new cell types to any other party on terms more favorable than those offered to Geron in the option exercise negotiation.¹⁷⁷ Further, Geron has a right to sublicense its licenses under the agreement.¹⁷⁸

At the same time, WARF has struck a good deal as well. It has had a chance to evaluate Geron as a commercializing entity for WARF's patents since 1996 and, presumably, has been pleased with Geron's progress. Keep in mind that TTOs have to place two bets when considering commercializing faculty research: the first is that the research, and its related technology, can ultimately result in successful products in the marketplace; the second is that the outside organization that the TTO selects to actually undertake the commercialization process, as licensee of the technology, can successfully execute on a good commercialization plan. WARF also got a grant back nonexclusive license to any enhancement or improvement patents that Geron develops under the agreement.¹⁷⁹ But it is perhaps the compensation provisions of the 1999 Geron License that really shine for WARF. Besides continuing the arrangement from the 1996 Geron License wherein Geron reimbursed portions of WARF's costs for prosecuting the patents, both domestically and abroad,¹⁸⁰ and securing presumably decent royalty rates (including minimum annual royalties and milestone payments),¹⁸¹ WARF negotiated for generous upfront payments from Geron, initially in the form of a combination of cash, 100,000 stock options to Geron stock, and 20,000 shares of Geron common stock.¹⁸²

The value of the equity portion of the upfront payment became much easier to calculate when the parties amended the agreement in October 1999 to flip the stock option portion of the equity payment into actual shares of Geron common stock.¹⁸³ The net result was a flat upfront equity payment of 92,000 shares of Geron common stock, most critically with a specific requirement that Geron file a registration statement with the SEC by October 8, 1999 to register such shares for unrestricted public trading.¹⁸⁴ On the date that this amendment became effective, Geron's common stock was trading on Nasdaq at around \$10.00 per share, thus the value of the equity payment to WARF was approximately \$920,000.00. Not bad, especially considering that there was a cash upfront payment as well. Additionally, in early 2000, Geron's common stock peaked at

¹⁷⁷ *Id.* at sec. 2(C).

¹⁷⁸ *Id.* at sec. 2(B).

¹⁷⁹ *Id.* at sec. 2(D).

¹⁸⁰ *Id.* at sec. 4(C).

¹⁸¹ *Id.* at sec. 4(D)-(E). The actual royalty rates, minimum annual royalty payments, and milestone payments have been redacted from Geron's SEC filing.

¹⁸² *Id.* at sec. 4(A). The cash payment amount has been redacted from Geron's SEC filing.

¹⁸³ Amendment to License Agreement by and between WARF and Geron Corp. (effective October 1, 1999), sec. 1, *reprinted in redacted form in* Geron Corp., Form 10-Q for period ending September 30, 1999 (filed with SEC on November 15, 1999).

¹⁸⁴ Under federal securities laws, unregistered shares are not freely tradable on national stock exchanges. This limits the liquidity of such shares, and hence also reduces their value because resale of the shares involves a more cumbersome process than working through a broker-dealer affiliated with a national stock exchange such as the New York Stock Exchange.

nearly \$80.00 per share, resulting in a valuation of WARF's stake at that time of approximately \$7.3M, assuming that WARF had not already sold part of that stake.¹⁸⁵

Those who are unhappy with Geron's exclusive license, can take some comfort in the fact that the 1999 Geron License does, of course, have termination provisions tied to the usual triggers such as failure to meet milestones specified in the agreement or make royalty or other contractual payments under the agreement.¹⁸⁶ Further, and most relevant for the discussion below, the agreement also contains the government rights clause included in the 1996 Geron License as outlined above.¹⁸⁷ Thus, to the extent that any of the Licensed Patents arose from federally funded research, the U.S. Government has a nonexclusive license to practice those patents for government purposes. Technically, this means that Geron cannot have an exclusive license to any such patents, despite the exclusive grant language in the 1999 Geron License. Of course this is a standard issue in technology transfer licenses, especially in the life sciences, where Bayh-Dole covers so many university patents because of the extent of federal funding of university life sciences research. So, few sophisticated licensees will feel that they have been duped because they executed an agreement specifying an exclusive license, only to have that grant effectively cut back by later in the document by a clause noting the possibility of a government non-exclusive license. Nonetheless, the possibility of a government non-exclusive license does impact the value of the otherwise truly exclusive license to the licensee and so the 1999 Geron License, like the 1996 Geron License, provides for a reduction in royalty rates and license fees in the event that the government asserts a license.¹⁸⁸

On the same date as the amendment to the 1999 Geron License was effective, October 1, 1999, WARF created WiCell as a not-for-profit, wholly owned subsidiary to administer further research, training, and distribution of the newly cultivated Thomson hESC lines.¹⁸⁹ WiCell claims that it was necessary to move hESC research off campus because of the "federal funding prohibition,"¹⁹⁰ likely referring to the NIH moratorium on funding hESC research while it sorted through the ethical, legal, and social implications of such work.¹⁹¹ Ironically, the moratorium itself seems to have been put in place largely *as a response* to Thomson's cultivation of the hESC line.¹⁹² Anecdotally, I have heard that WARF's and Wisconsin's interest in moving the research off campus was instead to keep new inventions from falling under Bayh-Dole. The truth may perhaps be

¹⁸⁵ At the close of business on Friday, June 9, 2006, Geron's common stock traded at \$6.76 per share. Hopefully WARF has already diversified its portfolio by selling off some of the Geron shares at an earlier date (and higher value) . . .

¹⁸⁶ License Agreement by and between WARF and Geron Corp., sec. 7 (executed May 5, 1999, effective April 23, 1999) *reprinted in redacted form in* Geron Corp. Form 10-Q for period ending September 30, 1999 (filed with SEC on November 15, 1999).

¹⁸⁷ *Id.* at sec. 14.

¹⁸⁸ *Id.*

¹⁸⁹ WiCell Research Institute, Special Cells Create Special Opportunities and Special Problems (PowerPoint slides on file with author).

¹⁹⁰ *Id.*

¹⁹¹ See Sean M. O'Connor, *Intellectual Property Rights and Stem Cell Research: Who Owns the Medical Breakthroughs?*, 39 NEW ENG. L. REV. 665, 671 (2005).

¹⁹² See *id.* at 670-671.

somewhere in between – faced with the sudden prospect of greatly diminished funding for hESC research while NIH sorted things out, Wisconsin and WARF may felt that it might as well keep new hESC completely outside of federal funding, and hence government rights to new inventions under Bayh-Dole, because the amount of new federal funding for the research would not justify giving up those rights. But arguments that Wisconsin and WARF wanted to keep cultivation of actual hESC lines outside of federal funding to cut off government rights are off key in one specific regard: Bayh-Dole only governs *patents* that arise under federally funded research, not physical property, or even, for that matter, other forms of IP such as copyrights or trade secrets.¹⁹³

Regardless of the true motivations for the creation of WiCell, the net result is that the organization now controlled the valuable Thomson hESC line for distribution under MTAs, together with a sub licensable license from WARF for the Thomson stem cell patents and presumably any relevant new patents or applications that might arise from Thomson's ongoing work. WiCell's stated mandate is to "share[] widely" the Thomson hESCs,¹⁹⁴ although again, public perception seems to be that WiCell is not in fact doing this. But, in WiCell's defense, the 1999 Geron License really restricts what activities by third parties that WARF, and therefore WiCell, can license or sublicense, respectively. But if a particular third party activity cannot be licensed or sublicensed as appropriate, without violating the terms of the 1999 Geron License, then WiCell likely cannot deliver Thomson hESCs to that third party either. Even if its license from WARF permitted this, the transfer would be of little use to the recipient if it could not legally use the cells anyway, without infringing WARF's patents.¹⁹⁵

Accordingly, outside of the 1999 Geron License which does not specify that Geron use Thomson cultured hESCs, WARF and WiCell seem to have undertaken a lease-license model for distributing the Thomson hESC technology platform. That is, no parties seem to have been licensed to practice the patents without also obtaining hESCs from WiCell, and no hESCs were distributed by WiCell without a sublicense to the patents.¹⁹⁶ Further, the controlling document for conveyance of the (leased) property and

¹⁹³ Although where a federal funding recipient deems some new proprietary item or process a trade secret, it may still fall under government rights if it is nonetheless patentable subject matter, and hence a subject inventions under Bayh-Dole. In other words, the federal funding recipient probably cannot elect to protect something as a trade secret just to evade U.S. government rights in a patentable invention.

¹⁹⁴ WiCell Research Institute, Special Cells Create Special Opportunities and Special Problems (PowerPoint slides on file with author).

¹⁹⁵ Although many suspect that university researchers are in fact routinely infringing third party patents in their research based either on ignorance of the patents or misguided belief that the patents simply do not apply to them legally or morally. See John P. Walsh, Charlene Cho, Wesley M. Cohen, *Roadblocks to Accessing Biomedical Research Tools* (presentation at CSIC/OECD/OEPM Conference, "Research Use of Patented Inventions" Madrid, Spain, 18-19 May 2006) available at <http://www.oecd.org/dataoecd/40/12/36816897.pdf>.

¹⁹⁶ Some concrete evidence of this exists in the 1999 Geron License itself where WARF permits Geron to sublicense the patents only to collaborators in Geron's internal research program, but if the collaborator requires hESCs, they must come from WARF under a negotiated MTA. License Agreement by and between WARF and Geron Corp., sec. 2(A)(iii) (executed May 5, 1999, effective April 23, 1999) reprinted in redacted form in Geron Corp. Form 10-Q for period ending September 30, 1999 (filed with SEC on November 15, 1999).

patent license appears to have been an MTA. In the early days following Thomson's announcement of the cultivation of his hESC line, the conditions for mutually reinforcing physical property and IP rights for WARF were probably pretty good: no one else was (publicly) in possession of such a cell line, generating substantial leverage for WARF and then WiCell from that end; and the '780 Patent could at least be argued to cover hESCs, while the hESC specific '806 Patent was already being prosecuted.

Nonetheless, WiCell's position received a tremendous boost from two sources in 2001. First, despite NIH's resolution of its concerns over hESC research leading to its issuance of hESC research guidelines and solicitation of funding proposals in 2000, President Bush announced on August 9, 2001 that no federal funding would go to any researchers working with hESCs derived from cell lines created after that date.¹⁹⁷ Somewhere between Thomson's 1998 announcement of what was supposed to be the first immortal hESC line and August 2001, a number of new hESC lines had apparently been created – so much so that President Bush could claim that there would be plenty of sources of hESCs for federally funded researchers to work from even while complying with his order.¹⁹⁸ One might wonder whether any of these were licensed under the '780 Patent, or whether, again, WARF believed that the '780 Patent did not cover hESCs, but rather only non-human primate embryonic stem cells. At any rate, the number of viable hESC lines quickly dropped in the months after the Bush Order, so that the NIH Human Embryonic Stem Cell Registry (the Registry) ultimately listed only 22 approved hESC lines.¹⁹⁹ However, those approved lines are controlled by a lower number of distinct sources – seven organizations to be exact, with one, MizMedi Hospital in South Korea currently “on hold” in the wake of the stem cell crisis in that country.²⁰⁰ Thus, currently there are only six sources of viable, approved hESCs in the world, with only three – WiCell, BresaGen in Georgia, and University of California, San Francisco – based in the United States.²⁰¹ This clearly dramatically increases the value of WiCell's lines, compared to a world in which new hESC lines could be created and used in federally funded research at any time.

The second major event for WARF and WiCell in 2001 was, of course, the issuance of the '806 Patent, which was clearly directed to hESCs, on March 13. Now, regardless of the interpretation of the scope of the '780 Patent's claims, WARF had established clear patent control over hESCs that has yet to be openly challenged. Thus, even providers of existing approved hESC lines in the Registry other than WiCell are likely now subject to WARF's patent rights and users of hESCs from those sources need to have a license from WARF or WiCell to work with those hESCs. Therefore, with these two developments in 2001, WARF and WiCell solidified their position as the dominant force in hESC research, based on a highly effective lease-license model. In fact, it is hard to overestimate the strength of WARF and WiCell's position in the field –

¹⁹⁷ See Sean M. O'Connor, *Intellectual Property Rights and Stem Cell Research: Who Owns the Medical Breakthroughs?*, 39 NEW ENG. L. REV. 665, 671-673 (2005).

¹⁹⁸ See *id.* at 672. The Administration estimated that 60 hESC lines were available at the time of the Order.
Id.

¹⁹⁹ See *id.* at 689.

²⁰⁰ See NIH Human Embryonic Stem Cell Registry available at <http://stemcells.nih.gov/research/registry/>.

²⁰¹ *Id.*

a realization that seems to have only been slowly dawning on many players in the field, including, perhaps, the forces behind Proposition 71 and the California Institute of Regenerative Medicine (CIRM) as evidenced by discussions during this Symposium. To be perfectly blunt, unless someone finds a way to successfully challenge or design around the '780 Patent and the '804 Patent, WARF and WiCell own the field. Further, even if a way is found around the patents, until Congress passes legislation to override the Bush Order, or Bush himself, or a future president, rescind the Order, researchers are still stuck with seven or fewer suppliers of hESCs approved for federally funded research. This has led to the state, federal, and local funding initiatives I have written about elsewhere.²⁰² But, the current hESC environment is an excellent case study for the stickiness of effective technology lease-license models based on mutually reinforcing physical property and IP rights: finding a way around one set of rights simply drives the person who wants to practice the technology freely headlong into the other set of rights. Accordingly, both sets of rights must be worked around, which is a far harder challenge than evading only one set.

Yet, all is not lost for the hESC researcher who wants to work with hESCs without signing an agreement with WARF/WiCell (at least directly). Returning to the government rights specifically listed in the '780 Patent and potentially existing in the '806 Patent, as outlined above, we find that the critical right mandated under Bayh-Dole is the nonexclusive license back to the government that must be included in funding agreements.²⁰³ I cannot stress enough that what I will call the 202(c)(4) license (after its section in the U.S. Code) is *completely different* from march-in rights that the funding agency can exercise only if the funding recipient has failed to commercialize the patent or other triggers occur.²⁰⁴ March-in rights are a bit of a red herring, in that they have received the lion's share of attention in the media as the key government right to federally funded patented inventions. But, they have still never been exercised and have only been contemplated a handful of times.²⁰⁵ On the other hand, the 202(c)(4) license requires no triggering event to become effective – other than the patenting of an invention arising out of the federally funded research – it is in place from the moment that the funding recipient executes the funding agreement because it is a required clause in such funding agreements.²⁰⁶ Thus, in the Thomson case, so long as the federal funding was given under a funding agreement executed after Bayh-Dole was passed, then the

²⁰² See Sean M. O'Connor, *Intellectual Property Rights and Stem Cell Research: Who Owns the Medical Breakthroughs?*, 39 NEW ENG. L. REV. 665, 674-681 (2005).

²⁰³ 35 U.S.C. § 202(c)(4).

²⁰⁴ 35 U.S.C. § 203.

²⁰⁵ See Sean M. O'Connor, *Intellectual Property Rights and Stem Cell Research: Who Owns the Medical Breakthroughs?*, 39 NEW ENG. L. REV. 665, 700-707 (2005).

²⁰⁶ I examine the 202(c)(4) government license in more detail in a forthcoming article in *The Maine Law Review* as part of an upcoming Symposium in Portland, Maine. See Sean M. O'Connor, *Public-Private Partnerships and De Facto Research Use Exemptions*, __ MAINE L. REV. __ (forthcoming 2007); see also Sean M. O'Connor, *Public-Private Partnerships and De Facto Research Use Exemptions: Case Study of the Thomson Stem Cell Patents* (presentation at CSIC/OECD/OEPM Conference, "Research Use of Patented Inventions" Madrid, Spain, 18-19 May 2006) available at <http://www.oecd.org/dataoecd/40/25/36817472.pdf>.

202(c)(4) license must be available to the government for its own use or for use on its behalf for government purposes.²⁰⁷

Despite the two open questions as to when the funding agreement was executed and whether the federal funding covered the research leading to the '806 Patent even though no government rights are listed in that patent, WARF, WiCell, and PHS²⁰⁸ all seem to agree that the 202(c)(4) license is in place for both the '780 Patent and the '806 Patent. Effective September 5, 2001 – thus after both the Bush Order and the issuance of the '806 Patent – WiCell and PHS entered into a Memorandum of Understanding (the WiCell-PHS Memo) that confirmed PHS's nonexclusive license to the '780 Patent and '806 Patent, as well as the patent application that led to the '252 Patent (deemed the "Wisconsin Patent Rights").²⁰⁹ The WiCell-PHS Memo also stipulates that PHS has no ownership rights in the actual hESC lines (deemed the "Wisconsin Materials").²¹⁰

But the fascinating aspect of the WiCell-PHS Memo is that it essentially undertakes to clearly authorize PHS contractors, who are none other than regular PHS extramural researchers at universities and other research institutions, to practice the Wisconsin Patents directly under PHS's license rights. At the same time, the WiCell-PHS Memo does not specifically use the term "license" nor reference the 202(c)(4) license by name which may lead to some confusion. One scholar at the Symposium in fact responded to a question about what led to the execution of the WiCell-PHS Memo by saying that PHS pressured WiCell into giving a license to the Wisconsin Patents under threat of march-in rights. But there is nothing in the record that I am aware of which would indicate that such pressure was brought to bear. Further, no justification for why march-in rights would have been able to be exercised in 2001 when the WiCell-PHS Memo was executed was given. Yet, a threat of march-in rights by a federal agency is not really credible unless the funding recipient has failed to take reasonable steps to commercialize the invention or otherwise triggered one of the specific bases for march-in rights. Further, if WiCell was bullied into giving a license that did not already exist, why is there no license grant in the WiCell-PHS Memo? Rather, the relevant language simply states that "The Parties agree that Wisconsin Patent Rights are to be made available without cost for use in the PHS biomedical research program subject to the following

²⁰⁷ Note that even though Bayh-Dole was passed in 1980, much research leading to currently patented inventions was funded before Bayh-Dole's passage. Even though many federal funding agreements before Bayh-Dole contained the nonexclusive license grant back to the government, not all did. See Sean M. O'Connor, *Intellectual Property Rights and Stem Cell Research: Who Owns the Medical Breakthroughs?*, 39 NEW ENG. L. REV. 665, 681-687 (2005). Thus, evidence of federal funding for, and thus government rights in, any particular patent must be examined to determine exactly when the funding agreement was executed and whether it contained a license clause if executed before Bayh-Dole's passage in 1980. This issue has arisen in the recent high profile litigation involving John Madey and Duke University. *Madey v. Duke University*, 307 F.3d 1351 (CA FC 2002); *Madey v. Duke University*, 336 F.Supp.2d 583 (MD NC 2004); *Madey v. Duke University*, 413 F.Supp.2d 601 (MD NC 2006).

²⁰⁸ As the parent agency of NIH, which funded the research noted in at least the '780 Patent.

²⁰⁹ Memorandum of Understanding between WiCell Research Institute, Inc. and Public Health Service, recital cl. 4 (effective September 5, 2001) available at <http://stemcells.nih.gov/research/registry/>. The application for the '252 Patent was U.S. Patent Application No. 09/522,030.

²¹⁰ *Id.* at recital cl. 5.

conditions . . .”²¹¹ Further, PHS’ funding of the Thomson research is said to have led to “certain *use* and other rights to the intellectual property.”²¹² No mention of a license is included in the subsequent conditions either, except for a license granted to third party suppliers of hESCs solely for them to provide the hESCs to PHS researchers.²¹³ This also serves to confirm the assertion above that particularly once the ‘806 Patent issued, all of the third party approved hESC providers were arguably infringing WARF’s patents.

All a PHS funded researcher need do under the terms of the WiCell-PHS Memo, is submit a completed version of the “Sample Simple Letter Agreement for the Transfer of Materials to PHS Scientists and PHS Contractors” (the Simple Letter Agreement) that was included as part of the WiCell-PHS Memo.²¹⁴ The Simple Letter Agreement is a basic form of a standard life sciences MTA. In fact, the combination of the master WiCell-PHS Memo document and the Simple Letter Agreement to record specific transfers of materials is somewhat similar to the Master UBMTA Agreement and its Implementing Letter form described above in Part I. No license grant is included in the Simple Letter Agreement, further reinforcing my argument that the whole arrangement between PHS and WiCell must be operating under the 202(c)(4) license, because no other license has been explicitly granted or would have arisen by operation of law or regulation like the 202(c)(4) license does.

Finally, the WiCell-PHS Memo underscores the lease-license model used by WiCell because it makes clear in both the master document and the Simple Letter Agreement that “Wisconsin Materials are the property of WiCell and are being made available to investigators in the PHS research community as a service by WiCell. Ownership of Wisconsin Materials shall remain with WiCell.”²¹⁵ Further restrictions on the use of Wisconsin Materials are included as well, in part to reinforce WARF’s exclusive IP license to the therapeutic and diagnostic fields (by prohibiting use of Wisconsin Materials in these fields by PHS contractors and limiting all uses to teaching and non-commercial research purposes), and in part to provide the liability limiting function discussed in Part I above.²¹⁶

In the end, the WiCell-PHS Memo is perhaps most intriguing for its clear demonstration that a government agency can make good use of the often-overlooked 202(c)(4) license. This is especially important in the hESC context because it shows that there are effective counterbalancing government rights to give researchers access to federally funded inventions even where patents and exclusive licenses otherwise seem to have locked down the field. Indeed, outside of this PHS research license bubble or zone, WiCell and WARF are widely believed to have been very tight with granting licenses

²¹¹ *Id.* at sec. 1.

²¹² *Id.* at recital cl. 4 (emphasis added).

²¹³ *Id.* at sec. 1(c).

²¹⁴ *Id.* at 8-9.

²¹⁵ *Id.* at sec. 2(a). It is unclear whether the inclusion of the term “service” is meant in the sense we used it above – e.g., personal or professional services – or whether it is being used in the sense of a public benefit or moral duty. If the former, then WiCell is claiming a service-license model that has even more implications for the legal rights of PHS and its researchers as set forth above in Part I.

²¹⁶ *Id.* at sec. 2.

even for research purposes. Of course, this PHS research bubble/zone is itself limited by the Bush Order. At the same time, WiCell has made it clear that it intends to make its hESCs (and appropriate sublicenses to the Wisconsin Patents) widely available to non-commercial researchers through an MOU and Simple Letter Agreement format similar to the WiCell-PHS Memo arrangement.²¹⁷ And it has a separate MTA for industry research, which it claims to be willing to use in “nearly all fields.”²¹⁸ Of course, this aspect of its program must be limited by the terms of the 1999 Geron License. Nonetheless, WiCell successfully bid to become the host for the National Stem Cell Bank established by NIH.²¹⁹ Accordingly, it has committed to attempt to collect all 22 approved stem cell lines and make them available to all researchers for \$500.00 per line, apparently with a license to the Wisconsin Patent Rights included.²²⁰

III. WHERE DOES CIRM FUNDED RESEARCH FIT IN?

One of the most unhappy places in the country with regard to WiCell’s domination of the hESC terrain is California and the CIRM. In 2004, the primary obstacle to the state’s strong hESC research community seemed to be the Bush Order from 2001.²²¹ Thus, creative Californians sought to sidestep the federal funding restrictions by financing the research themselves through Proposition 71.²²² But it actually turned out that WARF’s patents – already issued before Proposition 71 was put on the ballot – were the real problem. California and the new CIRM seem to have been unprepared for this patent problem. Further, because Proposition 71 and CIRM were intended to fund exactly the kinds of research that would *not* be funded by NIH under the Bush Order, CIRM is more or less boxed out of co-funding research with NIH that would then bring California CIRM funded researchers within the PHS research license zone outlined at the end of Part II above. While Proposition 71 does not prohibit such co-funding situations, it does clearly steer CIRM grants towards hESC research that will not otherwise receive timely funding.²²³

Thus, CIRM now faces two basic avenues to pursue: first, fund researchers who essentially are working “earlier” in, or alternatively to, the current chain of hESC

²¹⁷ WiCell Research Institute, FAQs About WiCell’s Policies on the Use of its hESC Lines, *available at* http://www.wicell.org/uploads/media/NIH_FAQs.pdf.

²¹⁸ See WiCell Research Institute, Special Cells Create Special Opportunities and Special Problems (PowerPoint slides on file with author); WiCell Research Institute, FAQs About WiCell’s Policies on the Use of its hESC Lines, *available at* http://www.wicell.org/uploads/media/NIH_FAQs.pdf.

²¹⁹ See WiCell Research Institute, FAQs About WiCell’s Policies on the Use of its hESC Lines, *available at* http://www.wicell.org/uploads/media/NIH_FAQs.pdf.

²²⁰ See *id.* WiCell makes it clear that hESCs obtained from other providers may require a separate license to the Wisconsin Patent Rights, leading one to infer that such a license is included when one obtains the hESCs from WiCell. See *id.* Again, it is not clear how this squares with the 1999 Geron License, or with the strong sentiment in the hESC research community that WiCell is holding up research by stingy with licenses.

²²¹ See Sean M. O’Connor, *Intellectual Property Rights and Stem Cell Research: Who Owns the Medical Breakthroughs?*, 39 NEW ENG. L. REV. 665, 675-679 (2005).

²²² See *id.*

²²³ See *id.*

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research such that they will not be infringing the Wisconsin Patents even as they design around those patents to come up with pluripotent human stem cell lines that do not infringe the patent either; and second, pursue a *de facto* research use exemption possibly available to states and their agencies under the doctrine of sovereign immunity. Along the former avenue, Kenneth Taylor, Christopher Thomas Scott, and Henry Greely of the Stanford University Program on Stem Cells in Society discuss some promising approaches in a recent article in *Nature Biotechnology*.²²⁴ Along the latter avenue, I will be examining this mechanism more completely in a forthcoming article for the *Maine Law Review*'s 2006-2007 Symposium issue.²²⁵ Therefore, I will only briefly describe it here.

Beginning from the premise that it is truly a state agency, and not an independent legal entity, CIRM can arguably practice patents without authorization of the owner under the doctrine of sovereign immunity. This works because under federal law prospective plaintiffs cannot use the federal courts to sue individual states. At the same time, patent infringement suits are limited to federal courts because they arise under federal law. Therefore, patent owners cannot sue states for infringement. While this doctrine has been upheld by the Supreme Court,²²⁶ it has prompted some unsuccessful bills in Congress. Thus, to the extent that a state and/or its agencies began relying on this doctrine as a routine matter, we could expect to see attempts at Congressional legislation overriding this doctrine. But, as it is rooted in constitutional law, any such legislation might be itself overturned by the courts as unconstitutional. The more practical question though, is whether a state or its agencies could immunize contractors under this doctrine under the argument that the contractors have been authorized to produce certain goods or services on behalf of the state government or agency. If so, then CIRM may be able to establish grant recipients as performing work on behalf of the State of California, somewhat similar to how PHS has authorized its extramural researchers performing hESC research under PHS grants to act on behalf of PHS in this work, thus bringing them directly under the 202(c)(4) government license under Bayh-Dole.

If CIRM cannot successfully pursue any of these avenues, then it will be stuck with whatever license terms it can negotiate with WARF and/or WiCell, at least until the patent terms run out for the '780 Patent and '806 Patent. I still am unsure why this is perceived to be so much of an obstacle by California legal commentators, although that claimed difficulty seems to turn on the commercialization licenses that WiCell is admittedly more careful about granting²²⁷ – again largely because WARF already granted substantial exclusive commercialization licenses to Geron. But if it is really the commercialization license that is creating the hurdles to CIRM plans, and based on WiCell's own linkage of the commercialization license with the path to clinical trials,

²²⁴ Kenneth S Taymor, Christopher Thomas Scott & Henry T Greely, *The Paths Around Stem Cell Intellectual Property*, 24 NATURE BIOTECHNOLOGY 411 (April 2006).

²²⁵ See Sean M. O'Connor, *Public-Private Partnerships and De Facto Research Use Exemptions*, ___ MAINE L. REV. ___ (forthcoming 2007).

²²⁶ See *Florida Prepaid Postsecondary Educ. Expense Bd. v. Coll. Sav. Bank*, 527 U.S. 627, 635, 647 (1999).

²²⁷ See, e.g., Kenneth S Taymor, Christopher Thomas Scott & Henry T Greely, *The Paths Around Stem Cell Intellectual Property*, 24 NATURE BIOTECHNOLOGY 411, 411 (April 2006).

then I would suggest the potentially risky, and certainly unorthodox, strategy of using the non-commercial licenses as far as they will go, so to speak, and then relying on the Supreme Court's recent broad interpretation of the Hatch-Waxman regulatory review research use exemption under 35 U.S.C. § 271(e) in *Merck KGaA v. Integra Lifesciences I, Ltd.*²²⁸ Public adoption of this strategy by CIRM or others could well push Congress to amend the statute, but until it does so, this could be a perfectly legal path around the allegedly onerous, or practically unavailable commercialization licenses from WiCell.

IV. CONCLUSION: LOOKING BEYOND THE THOMSON PATENTS

I am confident that one way or another, CIRM will find a path around the perceived obstacles of the Wisconsin Patents. But, as argued above, it is not necessarily patents that pose the greatest hurdles to research over time. Instead, those hurdles are often thrown up by physical property rights, as controlled and enforced through MTAs. But, as also discussed above, MTAs and other mechanisms for controlling or enforcing physical property rights are primarily governed by state law, especially contract law. In the case of human biological materials, states have established constitutional, statutory, and/or case law that may limit downstream uses of such materials depending upon what kinds of informed consent or other permissions are given by the original donors upstream.

The absence to date of any significant donor issues in the approved hESC lines should not make us complacent to the potential problems on the horizon.²²⁹ With only 22 lines total, and all of those developed by only seven research organizations, we may simply have not had the kind of volume and long term experience with hESC lines that will allow donor issues to emerge. Thus, as CIRM continues to promulgate rules and regulations regarding hESC research programs in California, it would do well to consider planning for and implementing a comprehensive chain of title type of system for biological materials all the way from donation through inclusion in commercialized products. This may seem like an incredibly attenuated chain, with the materials passing through control by many different organizations, but that is exactly the point. By allowing different parties with very different goals to control the materials at different times along the road, there is a substantial risk of a downstream party using the materials in a manner inconsistent with the donor's consent. This seems to be especially true if and when the patent obstacles are overcome and a rush to obtain large quantities of donor materials such as oocytes.

Other presenters and papers in this Symposium have greater expertise in the legal and ethical issues involved in informed consent, so I will not attempt to recapitulate those issues here. Instead, I will conclude by focusing on the consent issue that I believe is the most directly linked with commercialization: the statement of proposed use of the materials in the consent form. For example, Advanced Cell Therapies (ACT) has already

²²⁸ 545 U.S. 193 (2005).

²²⁹ Only one donor seems to have exercised any rights that would effectively retract an approved hESC line. See NIH Human Embryonic Stem Cell Registry available at <http://stemcells.nih.gov/research/registry/>.

begun actively soliciting donors to supply oocytes. It uses an informed consent form that includes an explicit waiver of any donor rights in commercial benefits arising from research using the materials, but focuses on the use of the materials for scientific research, rather than, say, the eventual product R&D that will lead to a saleable product. Further, many human biological materials are collected in university or non-profit settings that align with the public's general sense of what constitutes scientific research. But, is the disclosure of potential commercialization in the context of a waiver to donor rights in commercial benefits enough to trigger a meaningful understanding in donors that their materials can be transferred to a for profit corporation for commercialization? In other words, do the standard informed consent forms play on the public's general unfamiliarity with how the chain of commercialization works? Put still another way, will women being asked to donate oocytes, an unpleasant and risky procedure, be more inclined to do so when they are told the eggs will be used for potentially life-saving medical research than if they were told that the eggs would be used to develop profitable products for a private corporation? None of this is meant to denigrate the role that for profit entities play in the commercialization chain. Rather it is about making a point about accurately managing expectations rather than possibly playing on them.

Therefore, I propose that CIRM establish a system to monitor, guide, and control the entire commercialization rights chain. The first stage would consist of consent forms and other documentation for the original oocyte donation to research units. The second stage would be MTAs and other documentation used to transfer the materials, or their derivatives, to applied or translational R&D units. The third and final stage would be MTAs and other documentation used to transfer the materials to manufacture, distribution, and sales units, as applicable. This list is not meant to be exclusive: other transfers may have to happen for specific commercialization efforts. But the list gives a rough sense of what I mean by creating a comprehensive title chain for the materials. Of course, such a chain will not perform its desired function unless realistic and accurate disclosures are given to donors in their informed consent forms. While I am not advocating erring on the side of unnecessarily scaring off donors, today I believe that we generally err to far on the other side of suggesting an overly romantic notion of donation to medical science for the benefit of humanity. At one level, this depiction may well be true. But at another, it may seem manipulative to donors who do not realize that their biological materials will simply wind up in the hands of a for profit corporation who will quite possibly make a fair bit of profit off of the materials, albeit in a highly derivate form. In sum, more disclosure, not less, about the commercialization process for hESC therapies, diagnostics, and research tools will likely head off unexpected and potentially problematic backlashes by donors who are willing to undergo pain and inconvenience so long as it is for a cause they understand and support.

Scott Tocher

From: Elizabeth Sholes [sholes@calchurches.org]
Sent: Thursday, June 15, 2006 4:34 PM
To: CIRM Nonprofit IP Regs Comments
Subject: Proposed regulations on ownership and benefits of stem cell research

Dear Friends at CIRM:

California Church IMPACT was a strong and active supporter of Proposition 71 inaugurating stem cell research. We were under no illusion that this path-breaking research was without commercial benefit to the participants; it's the nature of both research and medicine today. Intellectual Property is both a public good and a private benefit.

However, we want strongly to advocate to CIRM that the sweeping support for use of \$3 billion in taxpayer dollars must confer some responsibility to repay the common coffer in several ways. None of these is inimical to the IP benefits. Agreements have already been made; now we must deliberate on the fair and just amounts.

The proposed return of 25 percent after a threshold of \$500,000 is, we believe, insufficient return to the state. We agree with some of our consumer group allies that the threshold should be \$100,000 since it is not net, not gross, revenue.

As important as the return of investment to the public is the marketing of all drugs and therapies emerging from stem cell research at reasonable prices, and the state Attorney General must have oversight and access to be able to monitor and enforce that fairness. What good will the investment of our tax money do if the ultimate benefit eludes the taxpayers who financed and backed all the capital investment? Stem cell products must be kept affordable by reflecting the true development costs and our public investment in it. CIRM would treat a private investor wisely with adequate return on capital. There should be no reason to treat the public with any less care in either royalty payments or product access.

Despite the matter of proprietary information, the very existence of CIRM is unusual in its shared access to capital. For the sake of the common good, CIRM must make publicly-funded research available to the greatest extent possible in patent pools. This is essential to assure that discoveries are maximized in their development and application to real human beings with real diseases and disabilities.

We represent 1.5 million members of the mainstream progressive Protestant communities of faith. For many members, support of stem cell was a moral and ethical struggle as was the commitment of our state's financial resources. Our hope for cures - and our faith in you - outweighed concerns, and we urge you to maximize that very hard won public trust.

Thank you for your attention to these issues.

Sincerely

Elizabeth Sholes
Director of Public Policy
California Council of Churches/California Church IMPACT
4044 Pasadena Avenue
Sacramento, CA 95821
(916) 488-7300 ext.3
www.churchimpact.org

Scott Tocher

From: gregdane@yahoo.co0m
Sent: Monday, June 12, 2006 10:59 AM
To: CIRM Nonprofit IP Regs Comments
Cc: gregdane@yahoo.co0m
Subject: Intellectual Property Regulations for Non-Profit Organizations

Dear IP Task Force Members,

Californians overwhelmingly supported Prop 71 because they believed the promise of breakthrough stem cell research and a payback to the state that would finance it. Your proposed rules don't go far enough to ensure fair prices for all Californians.

The California Attorney General must be able to "march-in" and intervene in cases of "unreasonable pricing" of a Prop 71-funded drug or therapy by a licensee. Reasonable pricing reflects the true cost of development of the medicine and the public's investment, no matter if it provided all or part of the money.

There should be a patent pool to foster sharing of publicly funded research and to make discoveries more available.

There should be a lower threshold for when the state begins to recoup some of its investment. As the rules are now written, payback begins when net revenue to a grantee tops \$500,000. Because it's net revenue rather than gross, the threshold should be \$100,000.

California voters didn't write biotech a blank check. Keep your Prop 71 promises. Now!

Sincerely,

James Salter
1725 York Ave. N
Golden Valley, MN 55422

Scott Tocher

From: rfroome1@yahoo.com
Sent: Monday, June 12, 2006 9:11 AM
To: CIRM Nonprofit IP Regs Comments
Cc: rfroome1@yahoo.com
Subject: Intellectual Property Regulations for Non-Profit Organizations

Dear IP Task Force Members,

Californians overwhelmingly supported Prop 71 because they believed the promise of breakthrough stem cell research and a payback to the state that would finance it. Your proposed rules don't go far enough to ensure fair prices for all Californians.

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California voters didn't write biotech a blank check. Keep your Prop 71 promises. Now!

Sincerely,

Roberta Froome
5531 La Cuenta Drive
San Diego, CA 92124

Scott Tocher

From: hiyou@kornsnake.com
Sent: Sunday, June 11, 2006 9:40 AM
To: CIRM Nonprofit IP Regs Comments
Cc: hiyou@kornsnake.com
Subject: Intellectual Property Regulations for Non-Profit Organizations

Dear IP Task Force Members,

Californians overwhelmingly supported Prop 71 because they believed the promise of breakthrough stem cell research and a payback to the state that would finance it. Your proposed rules don't go far enough to ensure fair prices for all Californians.

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California voters didn't write biotech a blank check. Keep your Prop 71 promises. Now!

Sincerely,

charlene chauvaux
923 sheffield st.
cambria, CA 93428

Scott Tocher

From: markshiatsu@earthlink.net
Sent: Saturday, June 10, 2006 8:35 PM
To: CIRM Nonprofit IP Regs Comments
Cc: markshiatsu@earthlink.net
Subject: Intellectual Property Regulations for Non-Profit Organizations

Dear IP Task Force Members,

Californians overwhelmingly supported Prop 71 because they believed the promise of breakthrough stem cell research and a payback to the state that would finance it. Your proposed rules don't go far enough to ensure fair prices for all Californians.

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California voters didn't write biotech a blank check. Please keep your Prop 71 promises.

Sincerely,

Mark Pasley
3130 California Street
Berkeley, CA 94703

Scott Tocher

From: unodivididopor0@yahoo.com
Sent: Saturday, June 10, 2006 12:59 PM
To: CIRM Nonprofit IP Regs Comments
Cc: unodivididopor0@yahoo.com
Subject: Intellectual Property Regulations for Non-Profit Organizations

Dear IP Task Force Members,

Californians overwhelmingly supported Prop 71 because they believed the promise of breakthrough stem cell research and a payback to the state that would finance it. Your proposed rules don't go far enough to ensure fair prices for all Californians.

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California voters didn't write biotech a blank check. Keep your Prop 71 promises. Now!

Sincerely,

Rohan Sabnis
156 Sequoia Ct.
Claremont, CA 91711

Scott Tocher

From: bwp97@verizon.net
Sent: Saturday, June 10, 2006 8:23 AM
To: CIRM Nonprofit IP Regs Comments
Cc: bwp97@verizon.net
Subject: Intellectual Property Regulations for Non-Profit Organizations

Dear IP Task Force Members,

Californians overwhelmingly supported Prop 71 because they believed the promise of breakthrough stem cell research and a payback to the state that would finance it. Your proposed rules don't go far enough to ensure fair prices for all Californians.

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California voters didn't write biotech a blank check. Keep your Prop 71 promises. Now!

Sincerely,

Beverly Williamson-Pecori
158 Russets Circle
Bridgeville, PA 15017

15

Scott Tocher

From: jmlnd1@comcast.net
Sent: Saturday, June 10, 2006 8:02 AM
To: CIRM Nonprofit IP Regs Comments
Cc: jmlnd1@comcast.net
Subject: Intellectual Property Regulations for Non-Profit Organizations

Dear IP Task Force Members,

Californians overwhelmingly supported Prop 71 because they believed the promise of breakthrough stem cell research and a payback to the state that would finance it. Your proposed rules don't go far enough to ensure fair prices for all Californians.

The California Attorney General must be able to "march-in" and intervene in cases of "unreasonable pricing" of a Prop 71-funded drug or therapy by a licensee. Reasonable pricing reflects the true cost of development of the medicine and the public's investment, no matter if it provided all or part of the money.

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California voters didn't write biotech a blank check. Keep your Prop 71 promises. Now!

Sincerely,

John Lewis
780 S. Hillside Ave.
Elmhurst, IL 60126

Scott Tocher

From: sgberg@pacbell.net
Sent: Friday, June 09, 2006 11:28 PM
To: CIRM Nonprofit IP Regs Comments
Cc: sgberg@pacbell.net
Subject: Intellectual Property Regulations for Non-Profit Organizations

Dear IP Task Force Members,

Californians overwhelmingly supported Prop 71 because they believed the promise of breakthrough stem cell research and a payback to the state that would finance it. Your proposed rules don't go far enough to ensure fair prices for all Californians.

The California Attorney General must be able to "march-in" and intervene in cases of "unreasonable pricing" of a Prop 71-funded drug or therapy by a licensee. Reasonable pricing reflects the true cost of development of the medicine and the public's investment, no matter if it provided all or part of the money.

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There should be a lower threshold for when the state begins to recoup some of its investment. As the rules are now written, payback begins when net revenue to a grantee tops \$500,000. Because it's net revenue rather than gross, the threshold should be \$100,000.

Remember: It was the public who passed Prop 71, in the public interest.
Please ensure maximum protection for that interest.

Sincerely,

Stephen Greenberg
14 Turpentine Drive
Nevada City, CA 95959

Scott Tocher

From: mark@consumerwatchdog.org
Sent: Wednesday, May 31, 2006 10:56 AM
To: CIRM Nonprofit IP Regs Comments
Cc: mark@consumerwatchdog.org
Subject: Intellectual Property Regulations for Non-Profit Organizations

Dear IP Task Force Members,

Californians overwhelmingly supported Prop 71 because they believed the promise of breakthrough stem cell research and a payback to the state that would finance it. Your proposed rules don't go far enough to ensure fair prices for all Californians.

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California voters didn't write biotech a blank check. Keep your Prop 71 promises. Now!

Sincerely,

Mark Reback
1435 S Bundy Dr Apt 1
Los Angeles, CA 90025

Scott Tocher

From: ginacelio@gmail.com
Sent: Monday, May 29, 2006 3:26 PM
To: CIRM Nonprofit IP Regs Comments
Cc: ginacelio@gmail.com
Subject: Intellectual Property Regulations for Non-Profit Organizations

Dear IP Task Force Members,

Californians overwhelmingly supported Prop 71 because they believed the promise of breakthrough stem cell research and a payback to the state that would finance it. Your proposed rules don't go far enough to ensure fair prices for all Californians.

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California voters didn't write biotech a blank check. Keep your Prop 71 promises. Now!

Sincerely,

Georgina Celio
3342 Floral Meadow Drive
Bakersfield, CA 93308

15

Scott Tocher

From: darkbow47@evilemail.com
Sent: Thursday, May 25, 2006 6:15 PM
To: CIRM Nonprofit IP Regs Comments
Cc: darkbow47@evilemail.com
Subject: Intellectual Property Regulations for Non-Profit Organizations

Dear IP Task Force Members,

Californians overwhelmingly supported Prop 71 because they believed the promise of breakthrough stem cell research and a payback to the state that would finance it. Your proposed rules don't go far enough to ensure fair prices for all Californians.

The California Attorney General must be able to "march-in" and intervene in cases of "unreasonable pricing" of a Prop 71-funded drug or therapy by a licensee. Reasonable pricing reflects the true cost of development of the medicine and the public's investment, no matter if it provided all or part of the money.

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California voters didn't write biotech a blank check. Keep your Prop 71 promises. Now!

Sincerely,

Arthur Dauer
1119 SW 4th Ave #5
Gainesville, FL 32601

15

Scott Tocher

From: dodder@usc.edu
Sent: Monday, May 15, 2006 3:27 PM
To: CIRM Nonprofit IP Regs Comments
Cc: dodder@usc.edu
Subject: Intellectual Property Regulations for Non-Profit Organizations

Dear IP Task Force Members,

Californians overwhelmingly supported Prop 71 because they believed the promise of breakthrough stem cell research and a payback to the state that would finance it. Your proposed rules don't go far enough to ensure fair prices for all Californians.

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California voters didn't intend to write the biotech industry a blank check. We understood that the state would benefit from this research as well. A net revenue level of \$100,000 certainly seems reasonable to me.

Sincerely,

Danila Oder
530 S. Kingsley Dr. #402
Los Angeles, CA 90020

15
Scott Tocher

From: sarahkeech@yahoo.com
Sent: Saturday, May 13, 2006 8:30 AM
To: CIRM Nonprofit IP Regs Comments
Cc: sarahkeech@yahoo.com
Subject: Intellectual Property Regulations for Non-Profit Organizations

Dear IP Task Force Members,

Californians overwhelmingly supported Prop 71 because they believed the promise of breakthrough stem cell research and a payback to the state that would finance it. Your proposed rules don't go far enough to ensure fair prices for all Californians.

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California voters didn't write biotech a blank check. Keep your Prop 71 promises. Now!

Sincerely,

Sarah Keech
148 North Saint Andrews Place, Apt. 26
Los Angeles, CA 90004

15

Scott Tocher

From: npkelly@netzero.net
Sent: Friday, May 12, 2006 1:49 PM
To: CIRM Nonprofit IP Regs Comments
Cc: npkelly@netzero.net
Subject: Intellectual Property Regulations for Non-Profit Organizations

Dear IP Task Force Members,

Californians overwhelmingly supported Prop 71 because they believed the promise of breakthrough stem cell research and a payback to the state that would finance it. Your proposed rules don't go far enough to ensure fair prices for all Californians.

The California Attorney General must be able to "march-in" and intervene in cases of "unreasonable pricing" of a Prop 71-funded drug or therapy by a licensee. Reasonable pricing reflects the true cost of development of the medicine and the public's investment, no matter if it provided all or part of the money.

There should be a patent pool to foster sharing of publicly funded research and to make discoveries more available.

There should be a lower threshold for when the state begins to recoup some of its investment. As the rules are now written, payback begins when net revenue to a grantee tops \$500,000. Because it's net revenue rather than gross, the threshold should be \$100,000.

California voters didn't write biotech a blank check. Keep your Prop 71 promises. Now!

Sincerely,

Nancy Kelly
1624 E. Hedges Ave.
Fresno, CA 93728

15

Scott Tocher

From: cheshirecaaat@cox.net
Sent: Thursday, May 11, 2006 5:40 PM
To: CIRM Nonprofit IP Regs Comments
Cc: cheshirecaaat@cox.net
Subject: Intellectual Property Regulations for Non-Profit Organizations

Dear IP Task Force Members,

Californians overwhelmingly supported Prop 71 because they believed the promise of breakthrough stem cell research and a payback to the state that would finance it. Your proposed rules don't go far enough to ensure fair prices for all Californians.

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Sincerely,

christine gilbert
1236 chambord ct
oceanside, CA 92054

Scott Tocher

From: carolmarie@cox.net
Sent: Thursday, May 11, 2006 7:49 AM
To: CIRM Nonprofit IP Regs Comments
Cc: carolmarie@cox.net
Subject: Intellectual Property Regulations for Non-Profit Organizations

Dear IP Task Force Members,

Californians overwhelmingly supported Prop 71 because they believed the promise of breakthrough stem cell research and a payback to the state that would finance it. Your proposed rules don't go far enough to ensure fair prices for all Californians.

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Sincerely,

Carol Lowe
752 N Recker Rd
Mesa, AZ 85205

15

Scott Tocher

From: virginia.downs@ttu.edu
Sent: Thursday, May 11, 2006 5:43 AM
To: CIRM Nonprofit IP Regs Comments
Cc: virginia.downs@ttu.edu
Subject: Intellectual Property Regulations for Non-Profit Organizations

Dear IP Task Force Members,

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Sincerely,

Virginia Downs
3701 - 40th Street
Lubbock, TX 79413

15

Scott Tocher

From: mf5131@yahoo.com
Sent: Wednesday, May 10, 2006 9:32 PM
To: CIRM Nonprofit IP Regs Comments
Cc: mf5131@yahoo.com
Subject: Intellectual Property Regulations for Non-Profit Organizations

Dear IP Task Force Members,

Californians overwhelmingly supported Prop 71 because they believed the promise of breakthrough stem cell research and a payback to the state that would finance it. Your proposed rules don't go far enough to ensure fair prices for all Californians.

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Sincerely,

Maureen Fahlberg
1735 Teakwood St
Boulder City,, NV 89005

15

Scott Tocher

From: e@samuda.com
Sent: Wednesday, May 10, 2006 8:08 PM
To: CIRM Nonprofit IP Regs Comments
Cc: e@samuda.com
Subject: Intellectual Property Regulations for Non-Profit Organizations

Dear IP Task Force Members,

Californians overwhelmingly supported Prop 71 because they believed the promise of breakthrough stem cell research and a payback to the state that would finance it. Your proposed rules don't go far enough to ensure fair prices for all Californians.

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Sincerely,

Elisha Belmont
10491 cunningham
westminster, CA 92683

15

Scott Tocher

From: delina@mac.com
Sent: Wednesday, May 10, 2006 5:58 PM
To: CIRM Nonprofit IP Regs Comments
Cc: delina@mac.com
Subject: Intellectual Property Regulations for Non-Profit Organizations

Dear IP Task Force Members,

Californians overwhelmingly supported Prop 71 because they believed the promise of breakthrough stem cell research and a payback to the state that would finance it. Your proposed rules don't go far enough to ensure fair prices for all Californians.

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Sincerely,

Delina Roberts
100 w. 5th St. #3G
Long Beach, CA 90802

15

Scott Tocher

From: jacques@asymtech.com
Sent: Wednesday, May 10, 2006 4:39 PM
To: CIRM Nonprofit IP Regs Comments
Cc: jacques@asymtech.com
Subject: Intellectual Property Regulations for Non-Profit Organizations

Dear IP Task Force Members,

Californians overwhelmingly supported Prop 71 because they believed the promise of breakthrough stem cell research and a payback to the state that would finance it. Your proposed rules don't go far enough to ensure fair prices for all Californians.

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Sincerely,

Jacques Couture
924 Carl Road
Lafayette, CA 94549

Scott Tocher

From: kid_keenan@yahoo.com
Sent: Wednesday, May 10, 2006 3:53 PM
To: CIRM Nonprofit IP Regs Comments
Cc: kid_keenan@yahoo.com
Subject: Intellectual Property Regulations for Non-Profit Organizations

Dear IP Task Force Members,

Californians overwhelmingly supported Prop 71 because they believed the promise of breakthrough stem cell research and a payback to the state that would finance it. Your proposed rules don't go far enough to ensure fair prices for all Californians.

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Sincerely,

Michael Keenan
339 West Tenth Street
Claremont, CA 91711

15

Scott Tocher

From: mbutler@thegrid.net
Sent: Wednesday, May 10, 2006 3:39 PM
To: CIRM Nonprofit IP Regs Comments
Cc: mbutler@thegrid.net
Subject: Intellectual Property Regulations for Non-Profit Organizations

Dear IP Task Force Members,

Californians overwhelmingly supported Prop 71 because they believed the promise of breakthrough stem cell research and a payback to the state that would finance it. Your proposed rules don't go far enough to ensure fair prices for all Californians.

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You are ethically required to make sure that the regulations implement the intent of Prop 71.

Sincerely,

Sandusky Shelton
PO Box 2397
Portola, CA 96122

15

Scott Tocher

From: Jeff@Barnard.net
Sent: Wednesday, May 10, 2006 3:08 PM
To: CIRM Nonprofit IP Regs Comments
Cc: Jeff@Barnard.net
Subject: Intellectual Property Regulations for Non-Profit Organizations

Dear IP Task Force Members,

Californians overwhelmingly supported Prop 71 because they believed the promise of breakthrough stem cell research and a payback to the state that would finance it. Your proposed rules don't go far enough to ensure fair prices for all Californians.

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Sincerely,

Jeff Barnard
504 Eureka Avenue
Santa Rosa, CA 95403

15

Scott Tocher

From: stevekolnathan@sbcglobal.net
Sent: Wednesday, May 10, 2006 3:08 PM
To: CIRM Nonprofit IP Regs Comments
Cc: stevekolnathan@sbcglobal.net
Subject: Intellectual Property Regulations for Non-Profit Organizations

Dear IP Task Force Members,

Californians overwhelmingly supported Prop 71 because they believed the promise of breakthrough stem cell research and a payback to the state that would finance it. Your proposed rules don't go far enough to ensure fair prices for all Californians.

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Sincerely,

steve walworth
2948 hawkridge
la crescenta, CA 91214

15

Scott Tocher

From: evalou_e@hotmail.com
Sent: Wednesday, May 10, 2006 2:09 PM
To: CIRM Nonprofit IP Regs Comments
Cc: evalou_e@hotmail.com
Subject: Intellectual Property Regulations for Non-Profit Organizations

Dear IP Task Force Members,

Californians overwhelmingly supported Prop 71 because they believed the promise of breakthrough stem cell research and a payback to the state that would finance it. Your proposed rules don't go far enough to ensure fair prices for all Californians.

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Sincerely,

Lou Edwards
260 Crownpointe Dr
Vallejo, CA 94591

15

Scott Tocher

From: Brad Dre [brad.dre@cox.net]
Sent: Wednesday, June 14, 2006 10:13 PM
To: CIRM Nonprofit IP Regs Comments
Cc: Jerry@consumerwatchdog.org
Subject: Stemp cell "IP"

I'm upset that the taxpayers are getting the shaft again. It seems our government funds research to no end, especially for drugs, and yet we pay the highest prices in the world!

The situation with Prop 71 couldn't be more clear: the taxpayers are backing the bonds that are funding your research. The taxpayers therefore should reap the benefits of any "IP" sales. And, it's not good enough to promise, there must be real enforcement, and real sharing of the benefits of this program provided by the taxpayers of CA.

That's why I'm urging that you adopt at least these proposals:

The California Attorney General must be able to "march-in" and intervene in cases of "unreasonable pricing" of a Prop 71-funded drug or therapy by a licensee. Reasonable pricing reflects the true cost of development of the medicine and the public's investment, no matter if it provided all or part of the money.

There should be a patent pool to foster sharing of publicly funded research and to make discoveries more available.

There should be a lower threshold for when the state begins to recoup some of its investment. As the rules are now written, payback begins when net revenue to a grantee tops \$500,000. Because it's net revenue rather than gross, the threshold should be 100,000.

Sincerely,

Brad Dre
Vista, CA
760-758-4476

15

Scott Tocher

From: Jim Highfill [jphighfill@earthlink.net]
Sent: Wednesday, June 14, 2006 8:33 PM
To: CIRM Nonprofit IP Regs Comments
Subject: IP for Non-Profit Institutions Regulations

To CIRM:

Californians overwhelmingly supported Prop 71 because they believed the promise of breakthrough stem cell research and a payback to the state that would finance it. Your proposed rules don't go far enough to ensure fair prices for all Californians. To ensure access, drugs financed by public funds must be accessible and affordable. Some of the people who needs these drugs the most are the elderly, who are hit hard by high drug prices.

That is why the California Attorney General must be able to intervene in cases of "unreasonable pricing" of a Prop 71-funded drug or therapy by a licensee. Reasonable pricing reflects the true cost of development of the medicine and the public's investment, no matter if it provided all or part of the money.

There should be a patent pool to foster sharing of publicly funded research and to make discoveries more available.

There should be a lower threshold for when the state begins to recoup some of its investment. As the rules are now written, payback begins when net revenue to a grantee tops \$500,000. Because it's net revenue rather than gross, the threshold should be \$100,000.

Sincerely,

Jim Highfill
Winnetka, CA

jphighfill@earthlink.net
EarthLink Revolves Around You.

7/7/2006

15

Scott Tocher

From: Stuart Bechman [sbechman@sbcglobal.net]
Sent: Thursday, June 15, 2006 1:12 PM
To: CIRM Nonprofit IP Regs Comments
Subject: Public comment on Prop. 71 non-profit institutions regulations

Dear CIRM:

Californians overwhelmingly supported Prop 71 because they believed the promise of breakthrough stem cell research and a payback to the state that would finance it. When I voted for this proposition, my primary concern was about where any profits from the research might go and whether the taxpayers would be able to recoup our investment; and since the proposal neglected to address this issue, I talked extensively to the campaign promoters about ensuring that the taxpayers' risk would be protected. I am disturbed that the payback regulations that your organization has proposed appear to be heavily slanted towards protecting corporate profits over the public interest.

There are several things that you could do to make your proposed recommendations more fair. First, the California Attorney General must be granted the authority to be able to step in and intervene in cases of "unreasonable pricing" of any Prop 71-funded drug or therapy by a licensee. Reasonable pricing should reflect the true cost of development of the medicine and the public's investment. This rule should be in place for any drug or therapy that was entirely or partially developed with Prop 71 monies.

Second, there should be a patent pool to foster sharing of publicly funded research and to make discoveries more available.

Finally, there should be a lower threshold for when the state begins to recoup some of its investment. As your rules are now written, payback begins when net revenue to a grantee tops \$500,000. Because it's net revenue rather than gross, the threshold should be absolutely no more than \$100,000 - and ideally should start from the first dollar of net profit. And rather than a 25% return, the percentage return to the taxpayers should be a minimum of 50%.

Thanks for your consideration of my comments.

Sincerely,

Stuart Bechman
Simi Valley, CA
805-522-4524
sbechman@sbcglobal.net

7/7/2006

Scott Tocher

From: bricar107@sbcglobal.net
Sent: Friday, June 16, 2006 1:25 PM
To: CIRM Nonprofit IP Regs Comments
Cc: bricar107@sbcglobal.net
Subject: Intellectual Property Regulations for Non-Profit Organizations

Dear IP Task Force Members,

Californians overwhelmingly supported Prop 71 because they believed the promise of breakthrough stem cell research and a payback to the state that would finance it. Your proposed rules don't go far enough to ensure fair prices for all Californians.

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California voters didn't write biotech a blank check. Keep your Prop 71 promises. Now!

Sincerely,

Brian Zwetzig
107 Los Altos Ct.
Santa Cruz, CA 95060

Scott Tocher

From: KenHofmann@Adelphia.net
Sent: Saturday, June 17, 2006 6:09 AM
To: CIRM Nonprofit IP Regs Comments
Cc: KenHofmann@Adelphia.net
Subject: Intellectual Property Regulations for Non-Profit Organizations

Dear IP Task Force Members,

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Sincerely,

Kenneth Hofmann
42336 Seville Circle
Quartz Hill, CA 93536

13

Scott Tocher

From: geraldflan@gmail.com
Int: Thursday, June 15, 2006 3:26 PM
To: CIRM Nonprofit IP Regs Comments
Cc: geraldflan@gmail.com
Subject: Intellectual Property Regulations for Non-Profit Organizations

Dear IP Task Force Members,

Californians overwhelmingly supported Prop 71 because they believed the promise of breakthrough stem cell research and a payback to the state that would finance it. Your proposed rules don't go far enough to ensure fair prices for all Californians.

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Sincerely,

Jerry Flanagan
8200 Redlands Apt 217
Playa Del Rey, DC CA

Scott Tocher

From: geraldflan@gmail.com
Sent: Thursday, June 15, 2006 3:26 PM
To: CIRM Nonprofit IP Regs Comments
Cc: geraldflan@gmail.com
Subject: Intellectual Property Regulations for Non-Profit Organizations

Dear IP Task Force Members,

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Playa Del Rey, DC CA